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LVI.—AMEBIASIS CUTIS (ENDAMEBA HISTOLYTICA)

REPORT OF TWO CASES *

MARTIN F. ENGMAN, JR., M.D.
ST. LOUIS
AND
HENRY E. MELENEY, M.D.
NASHVILLE, TENN.

Ulceration of the skin said to be due to an ameba, in some cases identified as *Endameba histolytica,* has been reported from many parts of the world. Engman and Heithaus,[1] in 1919, gave the name "amebiasis cutis" to this condition. These reported cases fall into four groups with reference to their connection with other primary conditions: (1) those following the drainage of an amebic abscess of the liver (Heimburger)[2]; (2) those following the drainage of a lesion of the appendix or other areas of the lower portion of the intestine (Cole and Heideman)[3]; (3) those about the anus associated with amebic colitis (van Hoof),[4] and (4) those without any direct connection with the viscera.[1] In practically all of these cases, motile amebas were found in fresh preparations from lesions of the skin. In a few, the identification of the ameba has been confirmed to the satisfaction of the authors by fixed smears and sections of tissue. The published reports, however, often do not contain descriptions or illustrations of sufficient clarity to convince protozoologists that the lesions of the skin were produced by a pathogenic ameba.

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* Dr. W. H. Cole, Dr. Robert Elman, Dr. H. A. Bulger and Dr. G. H. Copher of St. Louis have permitted us to report these cases.

* From the Department of Dermatology and Syphilology, Washington University School of Medicine, and the Department of Preventive Medicine and Public Health, Vanderbilt University School of Medicine.

* The Department of Pathology of the Vanderbilt University School of Medicine prepared many of the sections and the photomicrographs from both cases. Miss Susan Wilkes of Vanderbilt University furnished the colored drawings.

1. Engman, M. F., Sr., and Heithaus, A. S.: Amebiasis Cutis, J. Cutan. Dis. **37**:715 (Nov.) 1919.

2. Heimburger, L. F.: Amebiasis Cutis, Arch. Dermat. & Syph. **11**:49 (Jan.) 1925.

3. Cole, W. H., and Heideman, M. L.: Amebic Ulcer of the Abdominal Wall Following Appendectomy with Drainage, J. A. M. A. **92**:537 (Feb. 16) 1929.

4. van Hoof, L.: Abcès, fistules et ulcères d'origine amibienne, Ann. Soc. belge de méd. trop. **6**:45 (April) 1926; abstr., Trop. Dis. Bull. **23**:656 (Sept.) 1926.

For this reason, we have considered it important at the present time to report in detail two cases of amebiasis cutis which occurred recently in St. Louis and in which typical forms of *Endameba histolytica* were found in the lesions of the skin.

REPORT OF CASES

CASE 1.—*History.*—G. F., a landscape gardener, aged 51, was admitted to the St. Louis City Hospital on Oct. 2, 1929. He was of slight build and was somewhat emaciated. He gave a history of colicky pains in the abdomen and vomiting of all food taken for six days. His bowels, however, had moved regularly twice daily up to the day of admission.

His past history revealed nothing essential except an uncomplicated appendectomy seven years previously and a history of an acute attack, similar to the present one, three months before admission. He said that in his previous attack he had been jaundiced.

Diagnosis.—A diagnosis of intestinal obstruction was made, and he was given dextrose, enemas, gastric lavage and intravenous injections of solutions of sodium chloride. Pain and distention disappeared, and he was soon taking a full diet. A complete examination of the patient revealed a pathologic gallbladder and a persistent annular filling defect at the hepatic flexure of the colon, which was diagnosed by the roentgenologist as a carcinoma.

Operation and Course.—On October 21, an operation was performed by Dr. Robert Elman. The abdomen was opened through an incision over the upper right rectus muscle. The gallbladder was grayish and adherent to the duodenum. There were apparently no stones. At the hepatic flexure of the colon there was a firm annular "growth" narrowing the lumen and partially perforating it at one point, as shown by a certain amount of redness, fibrin and adherent omentum. No nodules were felt in the liver or in the mesenteric glands. There were a few soft lymph glands in the adjacent omentum. Further exploration of the abdomen gave negative results. The lesion was mobilized easily and resected with the actual cautery. An end-to-end anastomosis was done without tension or soiling. A large catheter was inserted into the proximal portion of the colon to protect the anastomosis by allowing for the escape of fecal material and gases. The wound was closed in layers. The resected portion of the colon was opened and presented an extensive ulceration encircling the intestine. It was not as hard as one would expect a carcinoma to be, and several sections failed to show any malignant change.

The immediate postoperative course was quite uneventful, and the patient had a spontaneous movement of the bowels on the third day. On the seventh day, a serous discharge developed at the lower end of the incision, which in a few days broke down, and a frank fecal fistula developed. The fistula, however, gave no great concern. It gradually diminished in size, and the patient began to have normal movements of the bowels. After a few weeks he was up and about the ward.

About two months after the operation, the patient became suddenly worse. The wound became more painful, and the skin about the wound showed a beginning necrosis. This necrosis began in the lower portion of the wound about the fistula and spread peripherally with moderate rapidity, producing an uneven, gyrate border. Beyond this border there was an advancing halo of erythema. In a few days, a second fistula developed lateral to the fecal fistula. This was

believed to be duodenal. The discharge contained dark bile and was alkaline to litmus. Methylene blue (methylthionine chloride, U. S. P.), given by mouth, appeared a few minutes later in the discharge. Necrosis of the skin about the wound progressed slowly, and after about six weeks an area 6 cm. in diameter was involved.

At this time, the duodenal fistula closed and the ulceration about the fecal fistula began to show some signs of healing. More healthy looking granulations appeared. Improvement, however, was of short duration. The ulcer took on a dirty, indolent appearance, and peripheral extension of the necrotic process became somewhat more rapid. Pain in the ulcer became so exquisite that dressing it was a problem. Since there was considerable cramping pain in the abdomen after eating, an obstruction at the site of the operation was suspected, but a barium meal demonstrated that no obstruction existed.

On March 4, 1930, two weeks after the more rapid spread began, Dr. W. H. Cole examined pus from under the overhanging edge of the ulcer and found numerous actively motile amebas which contained red blood cells. Fecal material from the fistula was also found to contain them in great numbers.

Dr. Engman first saw the patient on March 8. At this time the ulcer had involved an area about 12 by 15 cm. in the right half of the abdomen. It had spread in various directions, forming an irregular border. The upper medial portion was least active, and there seemed to be no spread in this direction. The lower lateral portion was most active. The floor of the ulcer consisted of hills and valleys of dirty granulation tissue on which lay necrotic epithelium and débris. The border was heaped up and undermined, with an overhanging edge of dying skin. About the advancing edge was a halo of purplish-red erythema which passed through various lighter shades until it blended with normal skin. Pressure on the edge caused welling up of thick yellowish-white pus with a tinge of fresh blood. Pain from any handling was most intense. A biopsy was performed and on the same day 1 grain (0.065 Gm.) of emetine hydrochloride was given intramuscularly. Emetine was then withheld pending confirmation of the diagnosis.

Six days later, the patient was seen again, and it was noted that the ulcer had spread about 3 cm. in its lower lateral corner. Another biopsy was performed, and smears of pus for permanent staining were prepared. Again, numerous actively motile amebas were found in the fresh pus from under the edge of the ulcer. Figure 1 shows the appearance of the ulcer at this time.

Intensive intravenous treatment with emetine hydrochloride was then instituted with very satisfactory results. The ulcer began to heal rapidly, and in about seven weeks the fistula had closed and the ulcer had almost entirely healed. The patient was discharged from the hospital on April 24, six months after his operation.

On May 6, twelve days following his discharge, the patient was readmitted to the hospital, complaining of nausea, vomiting and diarrhea which had begun that day. He reported that he had been well during the interval. His bowels had moved normally, and he had gained some weight. A grayish area about 2 cm. in diameter was noted in the center of the scar of the former ulcer, but there was no discharge. There was also slight pain over the old incision. However, the patient's condition improved, and he was discharged five days later, having apparently recovered from his attack.

On June 5, the patient was admitted again to the hospital with severe pain all over the abdomen and gaseous distention. The onset had been sudden the day before. A diagnosis of intestinal obstruction was made and was demonstrated

by a barium meal to be at the hepatic flexure. Conservative treatment did not relieve the situation, and since the patient's condition was rapidly growing worse, an operation was performed on June 19.

When the abdomen was opened, peritonitis was found. The patient's condition grew rapidly more serious on the table, so an ileostomy was performed and the operative wound was closed with drains. The patient's condition became progressively worse, and after four days the old fistula broke down and began draining feces. On June 26, three days later, the patient died.

Unfortunately an autopsy could not be obtained.

Histologic Examination.—Smears from an Ulcer of the Skin: Smears were fixed wet in Schaudinn's fixative (saturated solution of mercuric chloride [60

Fig. 1 (case 1).—Appearance of the ulcer of the skin just before institution of treatment with emetine.

parts]; 95 per cent alcohol [30 parts]; glacial acetic acid [from 5 to 10 parts]), and were stained by Heidenhain's iron hematoxylin method. They showed an exudate consisting of polymorphonuclear leukocytes, lymphocytes, plasma cells and large mononuclear phagocytes, and strands of fibrin. Scattered irregularly through the smears singly and in groups were amebas with the typical structure of *E. histolytica* (fig. 2). A distinct cellular membrane was present, also a zone of poorly stained ectoplasm and a central area of deeply staining, finely granular endoplasm containing the nucleus, and sometimes vacuoles, red blood cells or cellular débris. The nucleus was always circular, or nearly so, containing a heavy peripheral layer of chromatin somewhat unevenly distributed, a small round solid karyosome centrally or subcentrally located, and pale-staining, finely granular

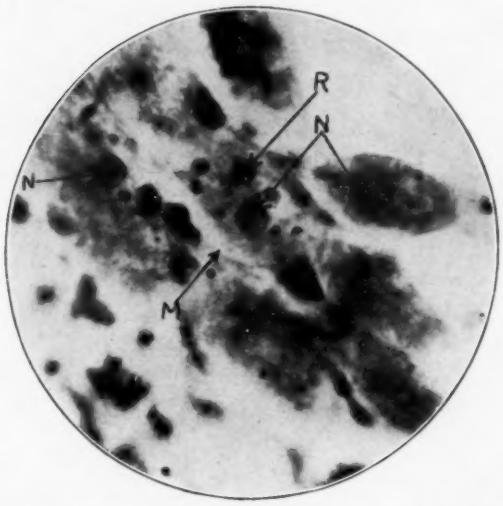


Fig. 2 (case 1).—Amebas in smear of pus expressed from the under edge of the ulcer of the skin. Fixation in Schaudinn's fluid, iron hematoxylin stain. Note the nuclear structure typical of E. histolytica. *N* indicates the nucleus of the ameba; *M*, the cell membrane of the ameba; *R*, a red blood cell; × 1,000.

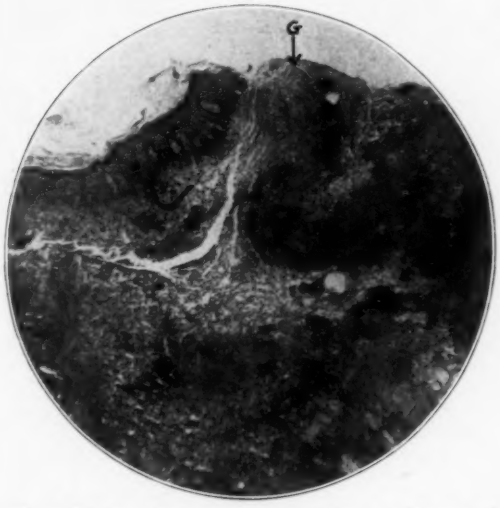


Fig. 3 (case 1).—Section from specimen taken at biopsy showing the edge of the ulcer of the skin. Note the eversion of the epidermis by the growth of granulation tissue (*G*), and the extension of the pathologic process beneath the epidermis.

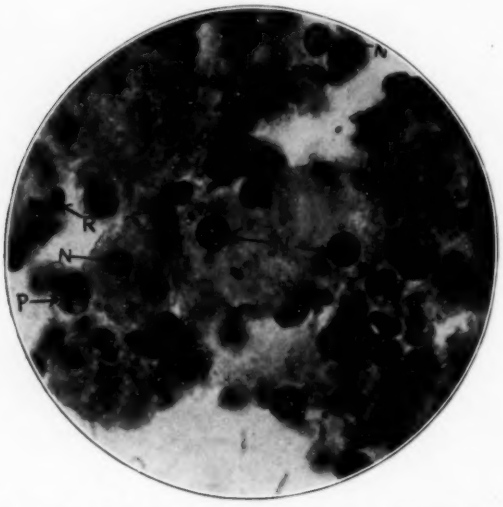


Fig. 4 (case 1).—Section from specimen taken at biopsy showing amebas in the pus on the surface of the ulcer of the skin. *N* indicates the nucleus of the ameba; *P*, a polymorphonuclear leukocyte; *R*, a red blood cell. Fixation in Zenker's fluid, phosphotungstic acid hematin stain; × 1,000.

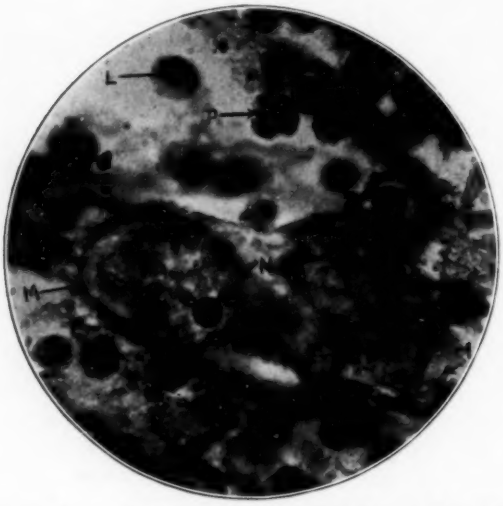


Fig. 5.—Same section as in figure 4. *N* shows the nucleus of the ameba; *M*, the cell membrane of the ameba; *P*, a polymorphonuclear leukocyte; *L*, a lymphocyte.

material. Occasionally there were a few dots of chromatin between the karyosome and the nuclear membrane. The amebas were frequently distorted by their position between strands of fibrin. Sometimes several lay close together almost like pavement epithelium. In their fixed condition they averaged about 25 microns in diameter. The nuclei measured from 4.5 to 5 microns in diameter.

Sections from Biopsy of an Ulcer of the Skin: The normal epidermis ended abruptly and was everted by the pathologic process and granulation tissue beneath it (fig. 3). The floor of the ulcer was covered with pus, consisting mostly of polymorphonuclear leukocytes, with a few mononuclear cells. Beneath this was granulation tissue infiltrated with all kinds of wandering cells and containing some hemorrhage. In some places there was a sharp line of demarcation between the surface pus and the granulation tissue. At a few localized points in the surface pus there were groups of amebas. In sections stained with Mallory's

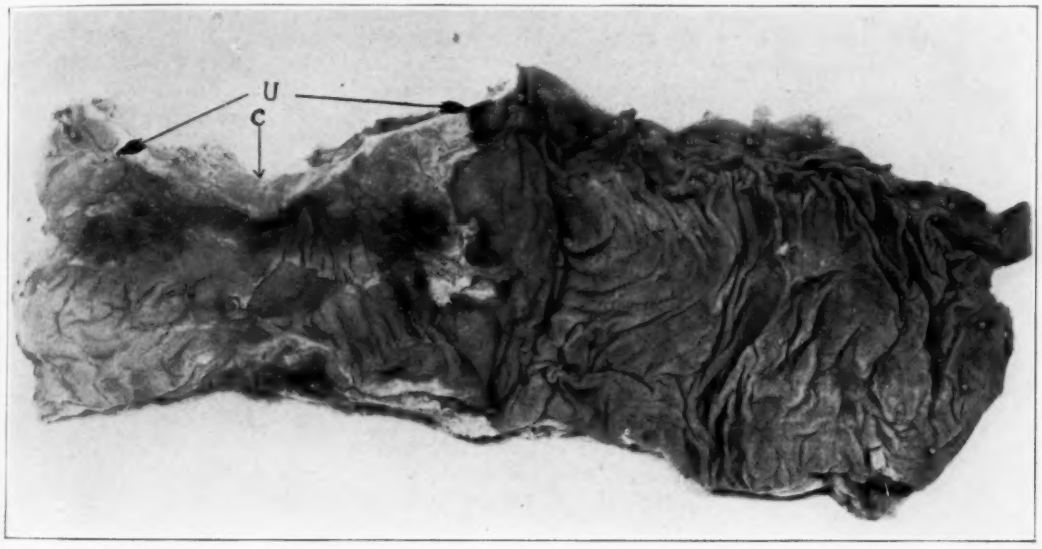


Fig. 6 (case 1).—Resected portion of the colon. *U* indicates the edge of the ulcer; *C*, the point of greatest constriction of the lumen. Note that the proximal (left) edge of the ulcer is inactive, while the distal (right) edge is active, with slough on the floor of the ulcer and erythema of the mucosa just beyond the overhanging edge.

phosphotungstic acid hematin, the amebas showed the same characteristics as those described in the smears, except that they were more circular in outline, had more coarsely granular and paler staining cytoplasm and usually did not show the distinction between ectoplasm and endoplasm (figs. 4, 5, 20 and 21). Some contained red blood cells.

Resected Colon.—The specimen of resected colon (fig. 6) fixed in formaldehyde was 17 cm. long. The distal portion, 10 cm. in length, was normal and measured 6 cm. in width on the mucosal surface. The proximal portion showed an ulcer with a constriction of the mucosal surface to a width of 3 cm. The ulcer at its proximal end had healed, leaving a flat, depressed surface about which the normal epithelium rose abruptly in an irregular outline. At the point of con-

striction, the healed scar entirely encircled the lumen. Beyond this, the surface was covered with a slough which became thicker until it met the overhanging edge of the mucosa in a fresh ulceration. Here the jagged border of the mucosa was raised and showed a red areola advancing somewhat beyond the ulceration. The wall of the intestine was considerably thickened from the constricted portion to the area of active ulceration, with the formation of fibrous tissue on the adventitial surface.

Microscopic examination of a section from the overhanging edge of this ulcer showed a normal epithelium abruptly terminated by coagulative necrosis. Beneath the epithelium, a necrotic process extended into the submucosa for a short distance, terminating in normal tissue. This tissue, as well as the area of necrosis, was heavily infiltrated with all varieties of wandering cells. On the surface of the ulcer beyond the epithelium was a layer of pus containing partly disintegrated fibrous tissue and leukocytes, mostly polymorphonuclear, with a high percentage of eosinophils. There were a few large mononuclear phagocytes. This layer of pus became thinner as it extended away from the edge of the ulcer. The submucosa was rather densely infiltrated with all kinds of wandering cells. No amebas could be definitely identified in the sections studied, though a few cells were present that resembled them in cytoplasmic structure. The nuclei of these cells were typical of amebas in size and shape, but were too faint for positive identification. This may have been due to the fixation of the tissue in formaldehyde. Dense colonies (clumps) of bacteria, mainly cocci, were present in the surface of the pus at some distance from the border of the ulcer.

Case 2.—*History.*—L. P., a white woman, aged 34, married, entered Barnes Hospital on Nov. 30, 1929, complaining of pain in the right upper quadrant of the abdomen. The history and complete examination of the case presented such a complicated picture that the diagnosis was anything but clear.

Her past history revealed only one essential point. Three years previous to admission, while on a trip to South America, she had had a "mucous colitis" lasting from four to five weeks with no recurrence.

For the past year the patient had been growing progressively "weak and draggy." She attributed the onset of her present illness to an attack of "grip" in September, 1929. At that time she had had aching pains in both sides of the chest and a temperature of 103.5 F., but very little cough and no sputum. In the right upper quadrant, just under the costal margin, she began having a dull aching pain which was continuous and formed her chief complaint on entering Barnes Hospital. She got up from her sickbed three weeks after the onset of her illness to move from New York to St. Louis.

Examination.—On admission to the hospital, the patient was subacutely ill. Her temperature was 38 C. (100.4 F.). She was pale and undernourished. Her heart was slightly enlarged to the left. There was a precordial thrill and a systolic and diastolic murmur at the apex. The abdomen showed a suggestive spasm of the upper right rectus muscle. The edge of the liver was two fingerbreadths below the costal margin and was tender. There was also tenderness in the right flank and the right costovertebral angle. The spleen was not palpable. The uterus was of the size of a gestation of from six to eight weeks.

Laboratory Examination.—The Wassermann and the Kahn tests of the blood were negative. The red blood cell count was 4,000,000 with 75 per cent hemoglobin. The leukocyte count was 9,000 with a practically normal differential picture. The blood sugar was 133 mg. per hundred cubic centimeters. The urine showed a trace of sugar. Roentgen examination of the chest gave negative

results. The preliminary impression was that the patient possibly had a subacute bacterial endocarditis with an unexplained hepatitis.

During the month following admission, the patient's condition gradually grew worse. The red blood cell count slowly dropped to 2,900,000 and the hemoglobin to 50 per cent. The leukocytes increased to 13,000 and the polymorphonuclear cells to 77 per cent. The temperature ranged from 38 to 39 C. (100.4 to 102.2 F.). A test for sugar tolerance revealed mild diabetes. Repeated cultures of the blood were negative. A cholecystogram showed no visualization of the gallbladder.

Because of the continued retrogression in the patient's condition, the lack of confirmatory evidence of bacterial endocarditis and an increase in the size and tenderness of the liver, an exploratory laparotomy was decided on.

Operation and Course.—On December 30, the operation was performed by Dr. G. H. Copher of the department of surgery of Washington University. The abdomen was opened by an incision over the upper right rectus muscle. The liver was found to be displaced to the left; it was dark red and was swollen, with rounded edges. The gallbladder showed evidence of early chronic cholecystitis. A mass could be felt in the upper right quadrant. Although the area was carefully walled off with gauze, it was ruptured in trying to ascertain the nature of the mass, and there was an escape of about 1 liter of thick, odorless pus. The exact position of the mass was not evident, but it was thought to be retroperitoneal. A stab wound was made into the flank below the costal margin for more dependent drainage, and the abscess cavity was also drained through the abdominal incision by rubber tubes and cigaret drains. Cultures, smears and guinea-pig inoculations of pus from the abscess were reported negative.

After the operation, the patient did moderately well for a few days. Almost at once, however, the skin about the wounds showed an erythema extending outward. There was a profuse drainage of dark, foul material, chiefly purulent. The erythema about the wounds spread with moderate rapidity, and twelve days after the operation the condition became alarming.

The edges of both wounds were gaping and showed some necrosis of the skin and the subcutaneous tissue. There was a zone of dusky redness about the wounds which gradually faded through different shades of red to the color of the normal skin. The patient was losing ground. The leukocyte count was 22,600, and the hemogram showed evidence of continued infection by an increase in "stab" and "juvenile" cells. An x-ray picture showed the right side of the diaphragm 3 inches (7.8 cm.) higher than the left.

On Jan. 16, 1930, sixteen days after the first operation, exploration of the wounds and the abscess cavity was performed by Dr. Copher. It was noted that necrosis of the wounds involved almost the entire thickness of the abdominal wall. The abscess cavity extended up to the diaphragm lateral to the liver. It was full of a very thick pus with a pungent sweetish odor. A biopsy from the edge of the anterior ulcer was obtained and showed numerous amebas in the necrotic tissue beneath the epidermis.

Necrosis of the anterior ulcer continued very rapidly until an area 4 inches (10 cm.) in diameter was involved. Amebas were not found at this time in direct smears either from the ulcer or from the pus in the abscess. Direct smears and cultures from the ulcer showed hemolytic streptococci and *Staphylococcus aureus*. On January 21, the patient died.

Autopsy.—An autopsy was performed by Dr. W. J. Siebert of the department of pathology of Washington University. There were two large, gangrenous foul-smelling ulcers in the right upper quadrant of the abdomen. The larger anterior

one led directly into an abscess in the peritoneal cavity lateral to the liver. The smaller one terminated in the abdominal muscles. The peritoneal cavity contained 300 cc. of cloudy fluid, and there was a fresh fibrinopurulent exudate on the serous coat of the intestines.

The abscess cavity, which was partially filled with foul-smelling material, extended above, behind, to the right of and in front of the right lobe of the liver. It was walled off from the general peritoneal cavity except at one point mesially, where the wall had become liquefied and opened into the peritoneal cavity. The abscess cavity was also connected by a wide opening with an abscess in the liver 6 cm. in diameter. This was the only large abscess in the liver. Its wall consisted of a necrotic grayish zone lacking a fibrous capsule. There were several small abscesses on the surface of the liver adjacent to the peritoneal abscess. Grossly the parenchyma of the liver appeared otherwise normal. The gallbladder was moderately thickened, and its contents could not be expressed by pressure.

The ascending colon contained a number of small, shallow ulcers, some with overhanging edges, others showing a gradual loss of epithelium, with a slightly necrotic surface.

The heart showed moderate stenosis and incompetence of the mitral valve and old verrucae on one cusp of the aortic valve. There were also fresh fibrinous deposits on both valves. There was a single anemic infarct in the right kidney. The lower lobe of the right lung was attached to the diaphragm by old fibrous adhesions and was partly atelectatic. The spleen was enlarged and soft. The uterus contained a male fetus 10 weeks old.

It is unessential to report the microscopic observations made at autopsy, except those of the abdominal ulcer, the liver and the intestine. Sections from these tissues and from the biopsy were furnished us for detailed study.

Biopsy.—The sections were fixed in formaldehyde and stained with hematoxylin and eosin.

Edge of the Ulcer of the Skin: At the edge of the ulcer, the virtually normal epidermis and the superficial cutis were raised up by an undermining necrotic process in the derma (fig. 7). This necrotic process extended deeply into the subcutaneous tissue. It was characterized by fragmentation of connective tissue fibers and infiltration by a moderate number of polymorphonuclear and mononuclear leukocytes. The process extended deeply into the subcutaneous tissue, sparing some of the sweat glands and penetrating between bundles of connective tissue. There were several collections of pus consisting mostly of polymorphonuclear leukocytes. Amebas were present in considerable numbers in one area of necrotic fibrous tissue and were also scattered singly through other necrotic areas. They were distinguished by their large size, definite cell membrane, finely alveolar or granular cytoplasm taking a blue stain and containing vacuoles and a small, round nucleus. The nucleus usually stained solidly deep blue, probably because of fixation in formaldehyde. Where the amebas were in groups, there was granular débris from destruction of tissue, but few wandering cells were present. A few bacteria were found on the surface of the ulcer, but none in the deeper tissues.

At the deepest portion of the section was a mass of fairly normal connective tissue containing several capillaries and larger blood vessels. In this area were many amebas, lying in the tissue spaces, in the lumina of the lymph capillaries (fig. 8) and in a necrotic thrombus partly occluding a vein (fig. 9). Some of these amebas contained red blood cells or black pigment precipitated in them by fixation in formaldehyde.

Autopsy.—Floor of the Ulcer of the Skin: Several sections from different locations showed essentially the same picture. Where the surface of the ulcer was shown,

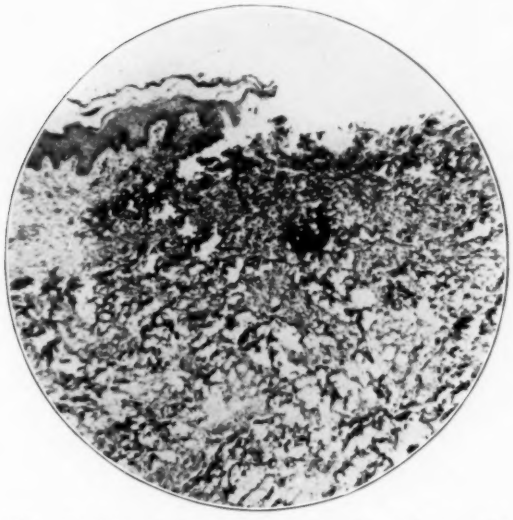


Fig. 7 (case 2).—Section of the ulcer of the skin taken at biopsy. Note the undermining of the epidermis, the lack of granulation tissue and the fragmentation of the connective tissue fibers in the derma. Fixation in formaldehyde, hematoxylin and eosin stain.

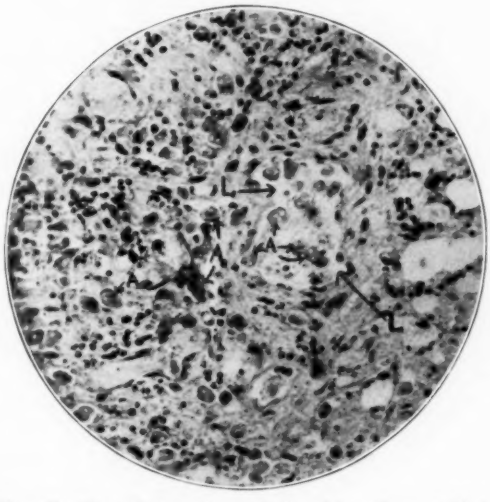


Fig. 8 (case 2).—Section of the ulcer of the skin taken at biopsy. Amebas are seen in and about a lymph vessel in the subcutaneous tissue beyond the area of necrosis. *L* indicates a lymph vessel; *A*, amebas.

it was covered either by normal granulation tissue or by a deep or shallow layer of slough over granulation tissue. The slough at its surface contained no cellular material, or only fragments of nuclei, but deeper it contained increasing numbers of polymorphonuclear and mononuclear leukocytes. The necrotic process involved the surface of the granulation tissue beneath it. A few amebas were scattered through the slough, more numerous at its base, and throughout the granulation tissue.

Sections from the subcutaneous fat and abdominal muscles beneath the ulcer showed superficial necrosis of the fat and connective tissue. Beyond this, the perivascular tissue was invaded by collections of lymphocytes and scattered large mononuclear phagocytes. Amebas were present in localized groups or scattered singly between fat cells or in the fat vacuoles of these cells (figs. 10 and 11). In the surface slough and in the fat tissue were collections of bacteria, mostly cocci

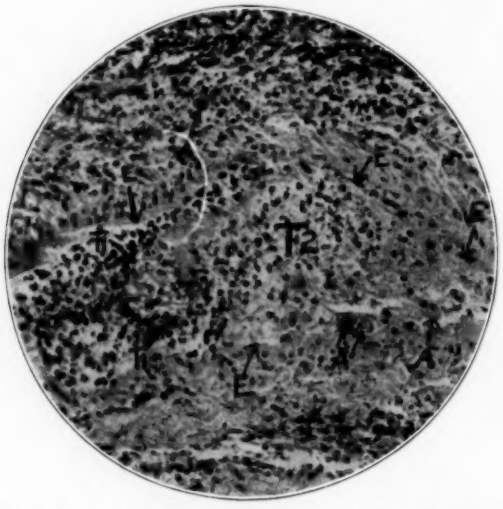


Fig. 9 (case 2).—Same section as in figure 8. There is thrombosis of a vein in the subcutaneous tissue, with amebas in the thrombus. T *1* indicates the free edge of the thrombus in the lumen of the vein; *T 2*, the body of the thrombus; *E*, the endothelium of the vein; *A*, amebas.

in chains and clumps. Where the pathologic process had advanced into the muscle tissue, there was progressive hyalinization and atrophy of the muscle fibers and invasion by large and small mononuclear leukocytes. In several bundles of muscles beyond the atrophied area, many amebas were found within the sarcolemma, sometimes two or more in one cell (figs. 12, 13 and 14).

Liver: The process here was typical of an amebic abscess of somewhat long duration. There was necrosis at the edge of the cavity of the abscess; beyond this there were atrophy of the parenchymatous hepatic tissue, infiltration of the remaining connective tissue with mononuclear leukocytes and a gradual transition to normal hepatic tissue. Amebas were present in large numbers in the necrotic area (fig. 14) and were found invading the atrophied hepatic tissue for a short distance (fig. 15). Many colonies of bacteria, mostly cocci in chains and clumps, were present in the necrotic border of the abscess.

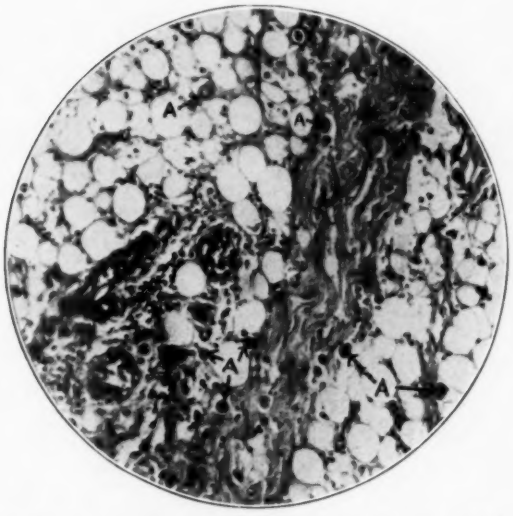


Fig. 10 (case 2).—Photomicrograph taken at autopsy, showing a section of subcutaneous fat with amebas (*A*) in relatively normal tissue. Fixation in Zenker's fluid; iron hematoxylin and eosin stain.

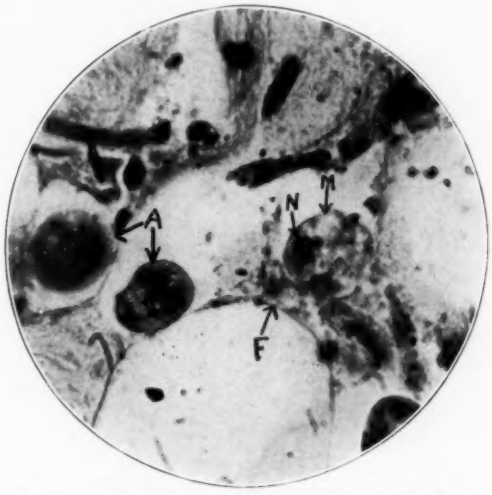


Fig. 11 (case 2).—Same section as in figure 10. *A* indicates amebas; *N*, the nucleus of an ameba; *M*, the cell membrane of an ameba; *F*, the outline of a fat vacuole; × 1,000.

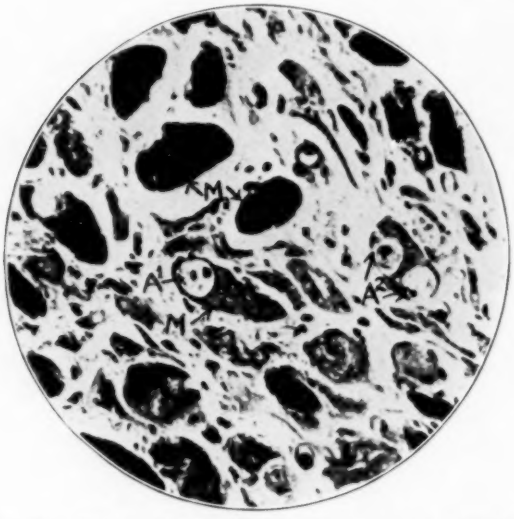


Fig. 12 (case 2).—Photomicrograph taken at autopsy, showing a section of abdominal muscle with amebas within muscle cells. *M* indicates muscle cells; *A*, amebas. Fixation in Zenker's fluid; iron hematoxylin and eosin stain.

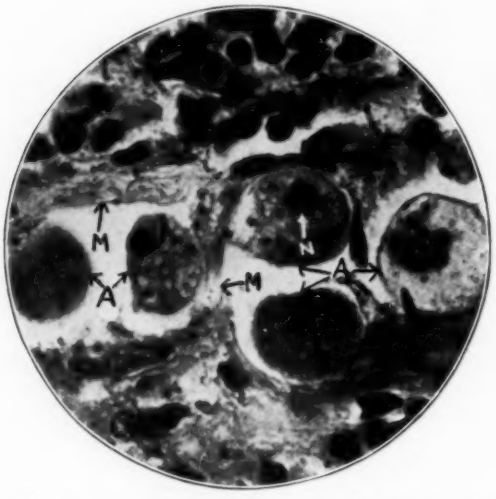


Fig. 13 (case 2).—Same section as in figure 10; two amebas in one muscle cell and three in another. *A* indicates amebas; *N*, nucleus; *M*, membrane of muscle cell; × 1,000.

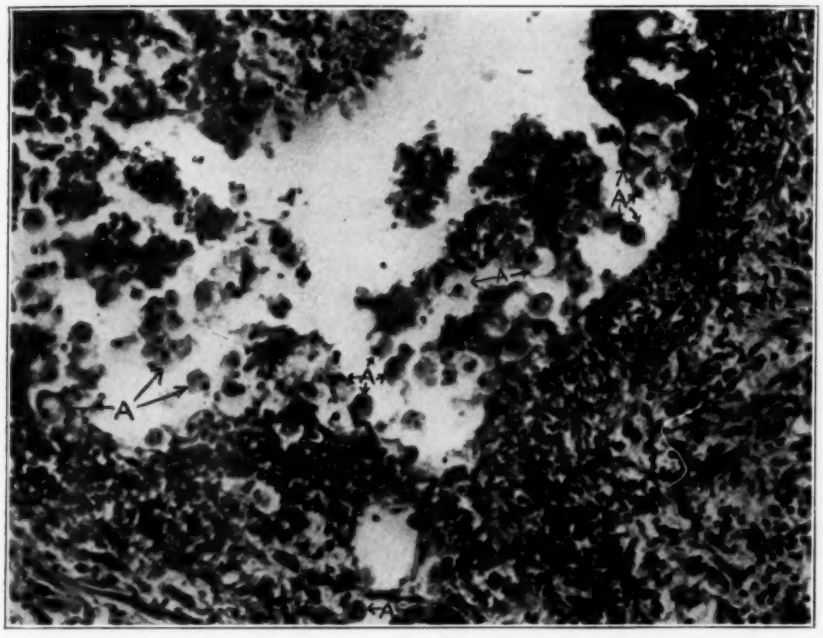


Fig. 14 (case 2).—Photomicrograph taken at autopsy, showing abscess of the liver. Amebas (*A*) are seen in the abscess cavity and in the adjacent atrophied hepatic tissue. Fixation in Zenker's fluid; iron hematoxylin and eosin stain.

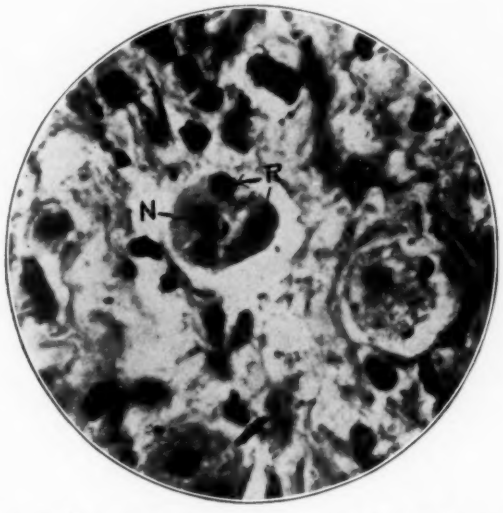


Fig. 15.—Same section as in figure 14. An ameba is shown in the atrophied hepatic tissue adjacent to the abscess. *N* indicates nucleus; *R*, phagocytosed red blood cells; × 1,000.

Colon: Several sections of the colon showed amebic ulcers in various stages of development. Most of them were small, and none extended deeper than the superficial part of the submucosa. One section showed two small ulcers with abrupt edges cutting through the epithelium and with some undermining (fig. 16).

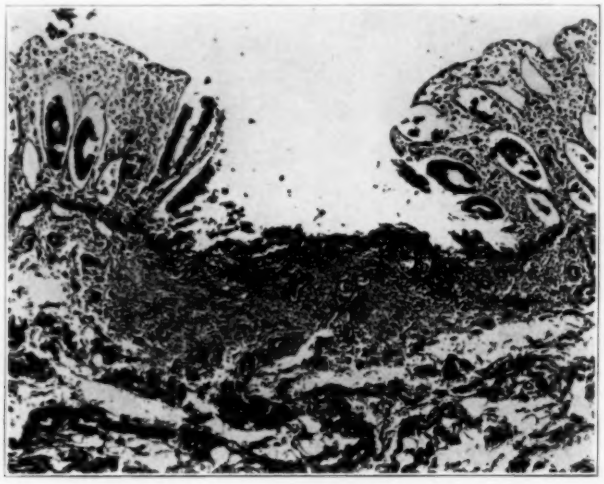


Fig. 16 (case 2).—Photomicrograph taken at autopsy, showing an amebic ulcer of the colon; note the overhanging edges.

Fig. 17 (case 2).—Photomicrograph taken at autopsy, showing the edge of early ulceration of the colon; note the gradual loss of epithelium.

In the other ulcers, there was undermining at one edge, but at the other the epithelium alone was first lost, leaving the stroma of the mucosa bare in the crypts, and then the villi were gradually lost, exposing the muscularis mucosae and, farther on, the submucosa (fig. 17). There were large numbers of amebas

Fig. 18.—Same section as figure 17. Amebas are seen in crypts of the mucosa.

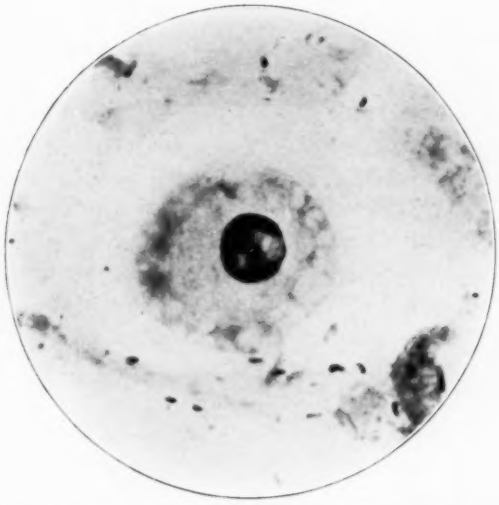


Fig. 19 (case 2).—Photomicrograph taken at autopsy, showing an ameba in a section of the ulcer of the colon. Note the nuclear structure typical of E. histolytica with crescentic peripheral chromatin and central karyosome. The ameba appears small in comparison with the size of its nucleus because it was not cut in its largest diameter. Fixation in Zenker's fluid; iron hematoxylin and eosin stain; × 2,000.

in the crypts of the mucosa where the epithelium was lost (fig. 18), and a few were present in the submucosa in the same region. Where the submucosa was exposed, there were usually scattered amebas in the tissue spaces and lymph vessels. This process was obviously in a very early stage of development, and was similar to the lesions described by Rees,[5] Kessel[6] and others in experimentally infected kittens.

Description of Amebas: The individual amebas found in the autopsy sections from all locations had the same general characteristics. The clearest pictures were obtained with iron hematoxylin counterstained with eosin. The amebas were circular or irregular, had a distinct cell membrane and cytoplasm which either stained diffusely and rather deeply with eosin, or stained faintly and was finely reticular or granular. Sometimes a clear ectoplasmic zone was visible, and often many vacuoles were present. Some amebas contained one or more red blood cells or particles of cellular débris. The nucleus was usually eccentric in position, was always circular or nearly so and varied in diameter from 4 to 6 microns. In the sections of intestine, most of the nuclei showed the typical structure of *E. histolytica*, with a peripheral rim of dense chromatin crescentically distributed and a small, circular subcentral karyosome (fig. 19). In sections from the abscess of the liver and the ulcer of the abdominal wall, it was more difficult to bring out the typical nuclear structure. Insufficient decolorization left a dense, black nucleus with iron hematoxylin and further decolorization often left only a pale peripheral rim of chromatin and failed to show the karyosome. Sometimes half of the nucleus would be decolorized, leaving the other half black. However, a sufficient number of satisfactorily stained amebas were found in each location to warrant the conclusion that they were *E. histolytica*. The colored plate shows camera lucida drawings of amebas from various locations.

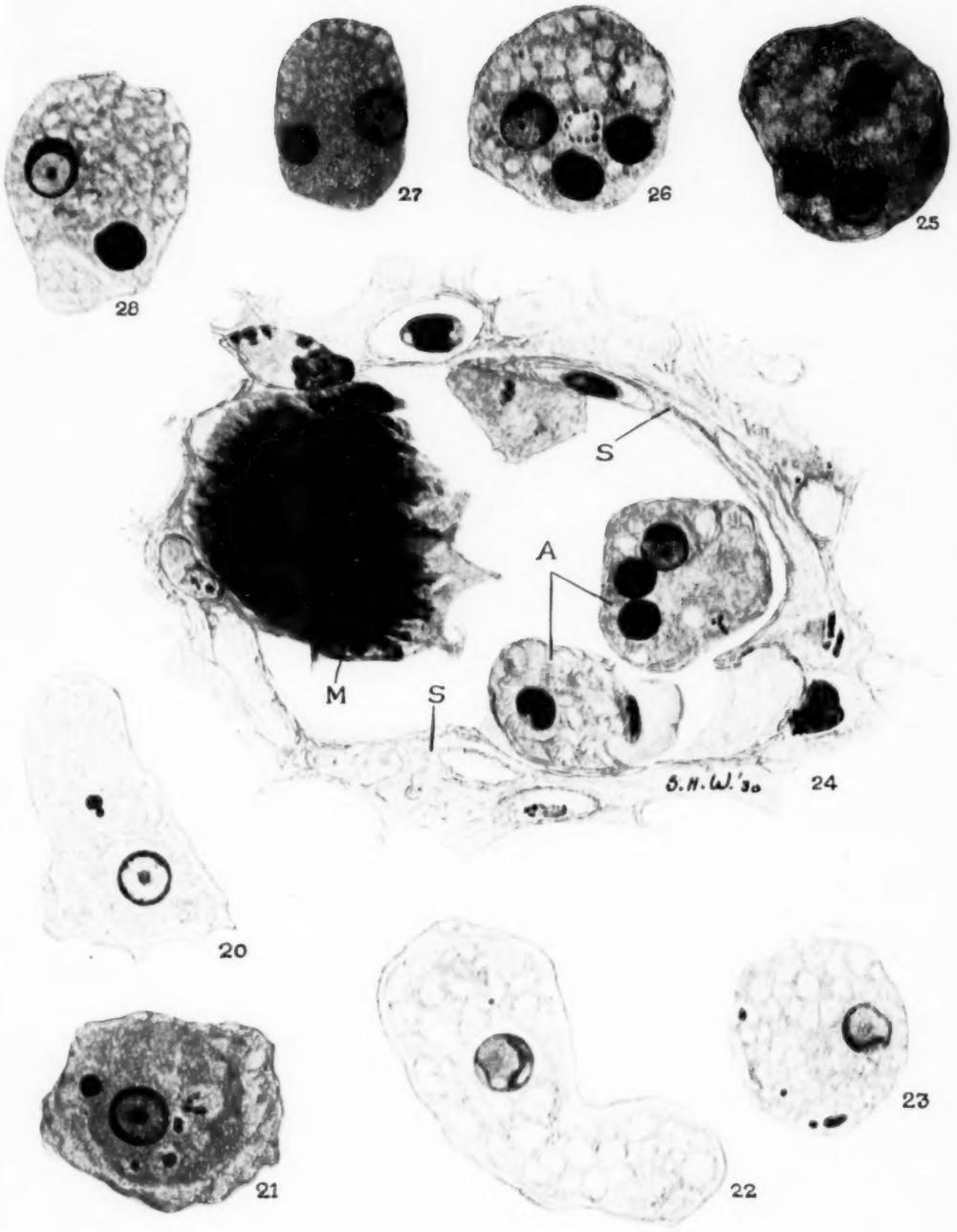
COMMENT

We believe that the evidence presented in both of these cases is sufficient to establish the identity of *Endameba histolytica* in the ulcers involving the skin and deeper tissues of the abdominal wall. Furthermore, the similarity between the histopathology of these lesions and of those in the liver and the intestine indicates that the ameba was of equal importance in producing the lesions in all of these locations. It is unfortunate that we were unable to make inoculations in animals, and cultures to complete the identification of the ameba and to further demonstrate its pathogenicity. These procedures should be followed in such cases in order to offer the most convincing proof of their amebic etiology.

The essential effect produced by *E. histolytica* on the tissues of the body is a lysis or dissolution without a marked reaction of the tissues

5. Rees, C. W.: Pathogenesis of Intestinal Amebiasis in Kittens, Arch. Path. **7**:1 (Jan.) 1929.

6. Kessel, J. F.: Amoebiasis in Kittens Infected with Amoebae from Acute and "Carrier" Human Cases and with the Tetranucleate Amoebae of the Monkey and of the Pig, Am. J. Hyg. **8**:311 (May) 1928.



Figs. 20-28.—All drawings were made with the camera lucida at a magnification of 1,500. The tissues were fixed in Zenker's solution. Figures 20, 22 and 23 were stained with Mallory's phosphotungstic acid hematin; the other figures were stained with iron hematoxylin and eosin. The different shades of red and brown in the latter figures are due to varying degrees of decolorization after the use of iron hematoxylin and to varying intensities of the eosin counterstain.

Figs. 20 and 21 (case 1).—Section from biopsy, showing amebas from the surface pus of the ulcer of the skin. Note the nuclei typical of E. histolytica and fragments of phagocytosed material.

Figs. 22 and 23 (case 2).—Sections at autopsy, showing amebas from the subcutaneous fat tissue. The nuclei are less typical because of difficulty in decolorization.

Fig. 24 (case 2).—Section at autopsy, showing atrophied striated muscle fiber of the abdominal wall invaded by two amebas, one of which contains two red blood cells. *M* indicates atrophied muscle substance; *S*, sarcolemma; *A*, amebas.

Figs. 25 and 26 (case 2).—Section at autopsy, showing amebas from the atrophied hepatic tissue adjacent to the abscess of the liver. Each ameba contains two phagocytosed red blood cells.

Figs. 27 and 28 (case 2).—Section at autopsy, showing amebas from ulcers of the colon. Each ameba contains one phagocytosed red blood cell.

except for the accumulation of a few wandering cells of the mononuclear varieties (Dobell and O'Connor [7]). When the surface of the tissue is exposed to bacterial contamination, the picture is complicated by the tissue reaction characteristic of a bacterial infection, which usually incites a polymorphonuclear reaction and the formation of frank pus. This picture is well illustrated in case 2 of this report. The early ulcers in the intestine and the presence of amebas in the relatively normal tissues of the abdominal wall beyond areas of necrosis represent the histopathology of uncomplicated amebic infection. The complicating picture of secondary bacterial infection is shown in the more superficial areas of the lesions of the skin where leukocytes are numerous and bacteria are present in abundance. When amebas are discharged in the pus from a lesion complicated with bacteria, they may, of course, be found on the surface or in granulation tissue which has developed in a healing portion of an older lesion, as in case 1. They may also produce a secondary necrosis in this granulation tissue, as occurred in case 2.

The essential characteristics of the clinical picture of amebic ulcers of the skin are: (1) a rapidly spreading ulcerative process, the activity of which varies in different portions of the margin; (2) a border that presents as a whole an irregular outline as a result of the varying rapidity of its progress; (3) an overhanging ledge of dying epidermis from under which pus may be expressed; (4) an advancing halo beyond the margin of the ulcer which varies in color from a dusky red through various shades until it merges gradually with the color of the normal skin; (5) pain and extreme tenderness on pressure; (6) the floor of the ulcer composed of indolent granulation tissue covered irregularly with débris and pus.

The relative importance of the ameba and of the bacterial infection in producing this clinical picture cannot be definitely stated at the present time. Rees [5] has shown that, in the kitten's intestine, *E. histolytica* apparently initiates lesions without the aid of bacteria or gross trauma, and a similar picture is seen in the intestine in case 2 of this report. In the initiation of the lesions of the skin in our cases, the surgical procedures made the tissues of the abdominal wall immediately exposed to invasion by both amebas and bacteria. The position of the amebas in the sections studied from case 2, where they were deep in the tissues in advance of bacterial invasion, indicates that the amebas were probably of primary importance in producing the lesions and that the bacterial infection was secondary. By inference, the same conclusion may be drawn from case 1, although the sections studied showed the amebas only in the surface pus.

7. Dobell, C., and O'Connor, F. W.: The Intestinal Protozoa of Man, New York, William Wood & Company, 1921.

In studying cases of ulceration of the skin in which the presence of amebas might be suspected, we believe that the first essential is the cooperation of a laboratory familiar with the minute characteristics of the intestinal protozoa and with the proper methods of demonstrating them. Fresh preparations of material pressed out from under the overhanging margin of the ulcer should be examined for motile amebas. If amebas are found, smears from the same location should be fixed wet in Schaudinn's fluid and stained with Heidenhain's iron hematoxylin. Specimens for biopsy should be taken from the advancing margin of the ulcer and preserved in a fixative suitable for the best nuclear staining, such as Zenker's or Bouin's solution, or some other mercurial fixative. Sections from these specimens should be stained with a good nuclear stain, such as iron hematoxylin or Mallory's phosphotungstic acid hematin. Cultures from favorable sites should be made on mediums suitable for growing amebas. If it is desired to further demonstrate the pathogenicity of the ameba, kittens may be inoculated by rectum with positive material, for the purpose of producing an acute amebic dysentery. The technic for carrying out these various procedures may be found in such textbooks as those by Zinsser [8] or Stitt,[9] and in more detail in papers by Boeck and Drbohlav,[10] Dobell and Laidlaw,[11] Rees,[5] Kessel[6] and others.

SUMMARY

1. Two cases are reported in which ulcers involving the skin and deeper tissue of the abdominal wall were found to contain amebas having the morphologic characteristics of *Endameba histolytica*. One was secondary to an operation for resection of a portion of the colon involved in an amebic ulceration. The other followed the drainage of an amebic abscess of the liver.

2. In case 1, typical *E. histolytica* were found in smears and sections from biopsy of an ulcer of the skin. The resected colon showed an old ulcerated process typical of amebiasis, but characteristic amebas were not absolutely demonstrable in the sections.

3. In case 2, typical *E. histolytica* were found in sections from biopsy of an ulcer of the skin and in autopsy sections from the floor of

8. Zinsser, H.: A Textbook of Bacteriology, ed. 6, New York, D. Appleton & Company, 1928.

9. Stitt, E. R.: Practical Bacteriology, Blood Work and Animal Parasitology, ed. 8, Philadelphia, P. Blakiston's Son & Company, 1927.

10. Boeck, W. C., and Drbohlav, J.: The Cultivation of Endamoeba Histolytica, Am. J. Hyg. **5**:371 (July) 1925.

11. Dobell, C., and Laidlaw, P. P.: On the Cultivation of Entamoeba Histolytica and Some Other Entozoic Amoebae, Parasitology **18**:283 (Sept.) 1926.

the ulcer, from the subcutaneous fat, from muscle tissue of the abdominal wall, from the abscess of the liver and from small ulcers in the colon.

4. No attempt has been made in this report to discuss the literature, as we considered it beyond the scope of this paper. However, attention is called to the fact that cases of this type should be studied by the most approved protozoologic methods, in order to establish beyond question their amebic etiology. Suggestions are made for carrying out such studies.

HETEROTHALLISM AMONG THE DERMATOPHYTES

AN INQUIRY INTO THREE OF THE COMMONER SPECIES *

DOROTHY SPRING, M.S.

PHILADELPHIA

This work was instigated by a paper written by Weidman entitled "Light from the Botanic Field on Medical Mycologic Problems." [1] The phase chiefly concerned was the remarkable morphologic variation within one and the same species of fungus; a variation that still persisted in hanging-drop cultures, even under the carefully controlled and uniform conditions that I have outlined in a preceding report.[2] It was thought that a study of heterothallism among the dermatophytes would lead to a better understanding of this variation.

REVIEW OF THE LITERATURE

Heterothallism may be defined as that property of certain fungi whereby two different cells (hyphae in our work), although identical morphologically, possess such different sexual properties that, on uniting, they can produce a new form. The presence of heterothallism may be demonstrated by taking a pure line strain, that is, a colony derived from a single cell of an organism, say *Neurospora crassa,*[3] and planting it adjacent to a similar pure line planting from the same species. These single cell strains are usually referred to as haplonts, and are free from male-female intermixture, being either purely male or purely female. As a result of this combination planting of the two haplonts, there may develop either (1) colonies producing only mycelium and conidia, products of nonsexual growth, or (2) highly specialized sexual reproductive organs, such as asci. By isolating rather large numbers of such haplonts and crossing them in all possible combinations,

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* From the Laboratory of Dermatological Research and the Laboratory of Hygiene, University of Pennsylvania.

* In partial fulfilment of the requirements for the degree of Doctor of Philosophy, Graduate School, University of Pennsylvania.

* Dr. Fred D. Weidman of the Laboratory of Dermatological Research personally supervised this work.

1. Weidman, F. D.: Light from the Botanic Field on Medical Mycologic Problems, Arch. Dermat. & Syph. **19**:867 (June) 1929.

2. Spring, D.: Morphological Variation Within the Same Species of Dermatophyte as Observed in Hanging-Drop Cultures, Arch. Dermat. & Syph. **23**: 1076 (June) 1931.

3. Shear, C. L., and Dodge, B. O.: Life Histories and Heterothallism of the Red Bread-Mold Fungi of the Monilia Sitophila Group, J. Agric. Research **34**:1019 (June 1) 1927.

each can be classified as one of two kinds that for convenience may be designated as A (male) and B (female) strains, depending on the production or nonproduction of asci. Mixtures of two A's or two B's will never result in the formation of asci. In the biologic sense, one strain simply possesses functional peculiarities that the other does not; there is a reciprocation between the two that may or may not be regarded as sexual, but that is of a sort to yield a new morphologic form. Thus heterothallism affords one explanation for morphologic variation within one and the same species.

However, heterothallism has been found to be by no means common among fungi; in fact, it is rather rare. Those species in which it does not exist are known as homothallic. Among the heterothallic fungi are found: *Rhizopus nigricans* (causing black mold of bread), numerous mucors, a large number of hymenomycetes (mushrooms and toadstools), some of the ascomycetes [4] (including *Neurospora sitophila* and *Neurospora crassa*). The neurospora named are red molds of bread once known as monilias; both were worked out by Shear and Dodge.[3] The most recent additions to this list are: certain species of *Dictyuchus* [5] and *Phytophthora* [6]; the smuts, *Ustilago levis* and *U. hordei*,[7] *U. zea* and *Sorosporium reilianum* [8]; and the rusts, *Puccinia helianthi*,[9] *P. graminis*,[10] *P. coronata* and *P. pringsheimiana*.[11] Nearly all of these are described by Gaumann,[4] and other references may be obtained from the recent publication of Ames.[12]

Extending to the bacteria and the blastomycetes, the work of Mellon [13] on heredity and Leonian's observations on mutation in phy-

4. Gaumann, E. A.: Comparative Morphology of Fungi, New York, McGraw-Hill Book Company, 1928.

5. Couch, J. N.: Heterothallism in Dictyuchus, A Genus of the Water Molds, Ann. Bot. **40**:849, 1926.

6. Narasimhan, M. J.: Studies in the Genus Phytophthora in Mysore: 1. Heterothallic Strains of Phytophthora, Phytopath. **20**:201 (March) 1930.

7. Dickinson, S.: Experiments on the Physiology and Genetics of the Smut Fungi, Hyphal-Fusion, Proc. Roy. Soc. **101**:126, 1927.

8. Hanna, W. F.: Studies in the Physiology and Cytology of Ustilago zeae and Sorosporium Reilianum, Phytopath. **19**:415 (May) 1929.

9. Craigie, J. H.: Experiments on Sex in Rust Fungi, Nature, London **120**: 116, 1927.

10. Craigie, J. H.: Discovery of the Function of the Pycnia of the Rust Fungi, Nature, London **120**:765, 1927.

11. Craigie, J. H.: On the Occurrence of Pycnia and Aecia in Certain Rust Fungi, Phytopath. **18**:1005 (Dec.) 1928.

12. Ames, L. M.: A Study of Some Homothallic and Heterothallic Ascomycetes, Mycologia **22**:318 (Nov.-Dec.) 1930.

13. Mellon, R. R.: Studies in Microbic Heredity: Sexuality (Zygospore Formation) in the Colon-Typhoid Group, J. Bact. **10**:481 (Sept.) 1925; The Sexual Cycle of B. Coli in Relation to the Origin of Variants with Special Reference to Neisser and Massini's Colimutabile, J. Bact. **10**:579 (Nov.) 1925.

tophthora [14] and fusaria [15] deserve attention along with those on heterothallism, because they broaden the approach to this subject of variation and supply systematic and definite avenues of inquiry. Leonian [15] recently found that a particularly dissociative form of fusarium was able to produce disease on young rhubarb plants in the greenhouse, whereas other variants from the same species were nonpathogenic. He did not work with single cell cultures, and heterothallism did not enter into consideration.

Under the heading of dermatophytes indicated in the title are grouped many species of fungi, almost exclusively *Fungi imperfecti* which are capable of inducing a superficial infection of animal skin. The disease, a form of ringworm known as dermatophytosis,[16] is exemplified by the more or less itchy inflammation between the toes that is popularly known as athlete's foot, but there are numerous other expressions of it.

METHODS AND MATERIAL

The immediate object of this work was to determine the presence or absence of heterothallism among the animal dermatophytes. In any case, single cell cultures were considered indispensable in order to draw any definite conclusions. To my knowledge, only one strain of the dermatophytes has been reported as being cultivated in single cell cultures. It was *Achorion gypseum* and was reported by Emmons [17] while this work was in progress. He obtained the same characteristic colonies from single "small conidia" (round spores or aleuries), as from single "macroconidia" (fuseaux).

For medical purposes, variations other than sexual (asci) are important. Hence observations as to heterothallism were made both grossly and microscopically. Grossly, evidences of heterothallism were watched for on the basis of such characters as luxuriance of growth, furrowing, craters, pigment and fluffiness or powderiness, as they appeared in gross cultures on dextrose agar. Hanging-drop cultures [2] were of the type customarily used in work with fungi, and were employed for studying the more detailed characteristics of the mycelium, and for diagnostic criteria such as aleuries, chlamydospores, fuseaux, spirals and engrappes.

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14. Leonian, L. H.: The Morphology and Pathogenicity of Some Phytophthora Mutations, Phytopath. **16**:723 (Oct.) 1926.

15. Leonian, L. H.: Studies on the Variability and Dissociations in the Genus Fusarium, Phytopath. **19**:753 (Sept.) 1929.

16. White, C. J.: Fungus Diseases of the Skin, Arch. Dermat. & Syph. **15**: 387 (April) 1927.

17. Emmons, C. W.: Observations on Achorion Gypseum, Mycologia **23**:87 (March-April) 1931.

Many methods have been recommended for obtaining single cells for culture. On account of the comparatively large size of the aleuries or spores, it was not necessary to use Chambers' micromanipulator,[18] which the bacteriologist employs for isolating single cells. The method of Dodge[19] for fishing single conidia from plate cultures was followed at first with some variations suggested by him personally.[20]

The aleuries employed were obtained from mature, characteristically powdery cultures on dextrose agar. We felt justified in using this rather than the corn meal agar of the botanist because it was on the dextrose mediums that the disturbing variations took place that prompted these studies. If this medium was adequate to induce heterothallic effects in our routine work, it should also do so in these especially planned tests for heterothallism.

Nevertheless, inquiry was made in a small way into the potentialities of corn meal agar, a medium that is especially useful because it restricts mycelial growth and is conducive to the formation of asci and perhaps other similar special sexual organs. Two plantings of each strain used in this work were made on slants of Difco corn meal agar, p_H 6.1. With one exception, the growth of all the strains consisted of a puny, loose white mycelium. *Trichophyton purpureum*, the exception, produced a growth of similar texture, but with an intense red coloration. Some of the pigment diffused into the surface strata of the medium. Nevertheless, microscopic examinations failed to reveal any of the special bodies in question.

Preliminary to planting, an emulsion was made of aleuries from a culture of dextrose agar in dextrose bouillon and was allowed to stand for at least twenty-four hours. Agar plates were poured, about 2 mm. in depth, using 4 per cent agar. On the surface of one of these about 2 cc. of dextrose bouillon (p_H 4.7) was poured; a loopful of the emulsion was added, and the plate was rotated in order to scatter the aleuries widely over the surface. The plates were left at the temperature of the room, the routine temperature for fungi, until the aleuries began to sprout, which occurred usually in about twenty-four hours.

Sprouting aleuries were easily seen under low-power magnification, and those that were in isolated positions were selected for transferring. The fishings were made with a fine platinum needle, slightly flattened on the end. Later in the course of the work, it was found that by pouring the plates 2 mm. deep, using dextrose agar (1.8 per cent), it was easy to "ring" a sprouting aleurie on the softer medium with a platinum loop. A straight needle was then used to remove it, taking the smallest possible amount of agar.

For a microscopic culture, the sprouting aleurie was placed at once into a hanging-drop of bouillon. This preparation was easily reexamined at frequent intervals to make sure at first that only one aleurie was present, and later to follow the course of development.

For making gross cultures, an intermediate agar plate was absolutely necessary in order to check up on the purity of the proposed pure line strain. The piece of agar containing a sprouting aleurie was placed on the surface of a plate poured from 4 per cent agar, of which previous mention was made. This was observed for at least two days to make sure that there were no other lagging, but still

18. Chambers, R.: New Micromanipulator and Methods for the Isolation of a Single Bacterium and the Manipulation of Living Cells, J. Infect. Dis. **31**:334, 1922.

19. Dodge, B. O.: Methods of Culture and the Morphology of the Archicarp in Certain Species of Ascobolaceae, Bull. Torrey Bot. Club **39**:139 (April) 1912.

20. Dodge, B. O.: Personal visit to the Laboratory of Dermatological Research.

living, aleuries concealed on the same piece of agar. The growth was then transferred to a dextrose agar slant. Care was taken during the whole course of this work to keep the piece of agar in such position that the colony was always on the upper surface where it would have access to oxygen. Ezekiel's [21] technic differed from this in that he planted the disks bearing single aleuries on the edge of the agar slant adjacent to the wall of the tube, so that they could be easily examined microscopically. There might be objections to this method in that nontypical colonies might develop as a result of the unequal balance of nourishment, part of the colony lying entirely on the glass wall of the tube.

TABLE 1.—*Single Cell* Cultures (Dextrose Agar Slants)*

	Reference Number	Total Number of Cultures Made	Matured		Died	
			Number	Per Cent	Number	Per Cent
Trichophyton interdigitale.....	1043	39	19	50	20	50
Trichophyton purpureum.....	1550	20	15	75	5	25
Trichophyton granulosum.....	2032	4	4	100	0	0
Trichophyton interdigitale.....	1894	17	16	94	1	6
Microsporon fulvum.....	1316	1	1	100	0	0
Total.....		81	55	68	26	32

* One aleurie.

TABLE 2.—*Single Cell Cultures (Hanging-Drops)*

	Reference Number	Total Number of Cultures Made	Matured		Died	
			Number	Per Cent	Number	Per Cent
Trichophyton interdigitale.....	1043	20	10	50.0	10	50.0
Trichophyton purpureum.....	1550	7	4	57.0	3	43.0
Trichophyton granulosum.....	2032	8	5	62.5	3	37.5
Trichophyton interdigitale.....	1894	10	6	60.0	4	40.0
Microsporon fulvum.....	1316	4	3	75.0	1	25.0
Total.....		49	28	57.0	21	43.0

Strains Used.—Four species of dermatophytes, including five strains, were used in these tests. *Trichophyton interdigitale* (no. 1043) and *Trichophyton purpureum* (no. 1550) have been described in a previous report.[2] *Trichophyton interdigitale* (no. 1894), powdery type, came from ringworm of the sole. *Trichophyton granulosum* Sabouraud [22] (our no. 2032), 1908 was also used; it came from a case of deep ringworm of the hand. Also *Microsporum fulvum* J. Uriburu,[23] 1907 (our no. 1316), which was isolated from a case of ringworm of the scalp, was used in some supplementary experiments. All of the trichophytons were recently isolated,

21. Ezekiel, W. N.: Modified Procedure with the Keitt Single-Spore Method, Phytopath. **20**:583 (July) 1930.

22. Pecus, M.: Une épidémie de trichophytie équine (800 cas); analyse mycologique par M. le Dr. Sabouraud, Rev. gén. de méd. vét., May 15, 1909, no. 154.

23. Uriburu, J. V.: Contribucion al estudio de las tinas en Buenos Aires, Argent. med., 1909, no. 42.

and, with the exception of *Trichophyton purpureum*, which had lost some of its pigment-producing properties, they showed no signs of pleomorphism when the work was begun.

Single Cell Cultures.—Before attempting the cross plantings involved in tests for heterothallism, it was necessary, of course, to secure the monospore strains (haplonts). Our experiences with this phase of the work will next be recorded.

The number of single cell cultures made, both gross and microscopic, with the results in each case, may be obtained from the tables (tables 1 and 2). Readings of the gross cultures were made and recorded at first weekly and later biweekly. Hanging-drops were examined sometimes twice daily for the first few days, after which they were observed once a week for two months or longer; records of progress of growth were kept by drawings. All the control cultures for this work, both gross and microscopic, were made in the usual manner by planting a small piece of culture material; these were read along with the single cell cultures.

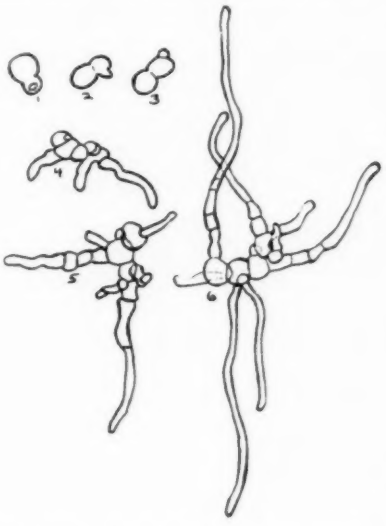

Fig. 1.—"Single cell" plant developing from an aleurie (Trichophyton interdigitale no. 1894. These drawings illustrate the extent of the observations made before regarding the colony as pure line: *1*, the cell at planting; *2*, five minutes later; *3*, sixty-five minutes after planting; *4*, eighteen hours after planting; *5*, twenty-six hours after planting, and *6*, thirty-six hours after planting.

RESULTS

Trichophyton interdigitale (no. 1043 and no. 1894).—Of the thirty-nine monospore (aleurie) plantings of the former no. 1043, on dextrose agar slants, only nineteen matured. The resulting colonies were flatter and more granular than the controls made from mixed, multicellular explants. None of the young cultures were ever quite as fluffy as *Trichophyton interdigitale* usually is at this stage, but this might readily be due to differences in the bulk of the material planted. The

old cultures showed a rather pale, typical café au lait tint, a flattening of the duvet and, in most cases, a marked degree of powderiness. The centers of all of these colonies were thrown up into short irregular folds or else were marked by deep depressions.

In addition to the foregoing gross cultures, twenty hanging-drop cultures were made from single aleuries; ten died and ten grew to full maturity; that is, they produced all the organs of fructification heretofore usually found in hanging-drops of this species.

As to the second strain of *Trichophyton interdigitale* (no. 1894), powdery type, of the seventeen dextrose agar plantings only one failed to mature. Sixteen showed typical growth, being flat and granular, and having a yellowish zone in the center. This strain grew rapidly, covering the entire slant in three weeks.

This high percentage of positive results is hard to explain; presumably it was due to greater vigor on the part of this strain. At least, the powderiness which featured the strain indicates a high capacity for production of reproductive structures (aleuries), and vigor in this direction might carry over into the resultant aleuries.

Of the ten hanging-drops made, six grew to maturity and produced the great variety of organes commonly found in hanging-drops of *Trichophyton interdigitale*. Of the four that died after sprouting, three purposely had been kept on an agar plate for a day and a half in the icebox at a temperature of about 2.7 C.; thereafter, the plate was kept, as usual, at the temperature of the room overnight preliminary to fishing the single aleuries.

Trichophyton purpureum (no. 1550.)—Of the twenty gross plantings, five failed to grow after the first sprouting. The fifteen that grew to maturity at first showed a white, rather fluffy growth, heaped up in the center. Later, the central part of the colony took on a pale creamy color and there were some indistinct radial furrows in the periphery. Finally, the growth became flatter and matted down, and a little pink coloring was produced on the under side of the colony where the mycelium touched the glass. In some cases, there was more of this coloring on the single cell cultures than on the control. The intense red coloration of the medium sometimes found in this species was lacking in all the cultures, including the control.

Of the hanging-drop preparations, four of seven grew to maturity and produced all the organes that were found in the controls. These aleuries grew so slowly that in one case it was possible to make a drawing showing the mother aleurie on the fourth day, and it could still be distinguished under the microscope on the sixth day.

Trichophyton granulosum (no. 2032).—All four of the single cell gross plantings of this strain grew and were almost identical in appearance with the control culture, except that the latter showed more pleomorphism (fluffiness).

TABLE 3.—*Mixed Cell Cultures (Dextrose Agar Slants)*

	Reference Number	Total Number of Cultures Made	Matured		Died	
			Number	Per Cent	Number	Per Cent
Trichophyton interdigitale.....	1043	4*	2*	50	2*	50
Microsporon fulvum.....	1316	6†	6†	100	0	0
Total.....		10	8	80	2	20

* Each planted with two aleuries.
† Each planted with one fuseau.

TABLE 4.—*Mixed Cell Cultures (Hanging-Drops)*

	Reference Number	Total Number of Cultures Made	Matured		Died	
			Number	Per Cent	Number	Per Cent
Trichophyton interdigitale.....	1043	6*	3*	50	3*	50
Trichophyton granulosum.....	2032	5*	4*	80	1*	20
		14†	5†	35	9†	65
		1‡	1‡	100	0	0
Microsporon fulvum.....	1316	4§	1§	25	3§	75
		1#	1#	100	0	0
Total.....		31	15	48	16	52

* Each planted with two aleuries.
† Each planted with one fuseau.
‡ Each planted with one fuseau and one aleurie.
§ Each planted with two fuseaux.
# Planted with two fuseaux and four aleuries.

TABLE 5.—*Comparison of Single and Mixed Cell Plantings*

	Per Cent Matured	Per Cent Died
Glucose agar slants		
Single cell.....	68	32
Mixed cell.....	80	20
Hanging-drops		
Single cell.....	57	43
Mixed cell.....	48	52

Of the eight hanging-drop cultures made from aleuries, five matured and three failed to grow.

MIXED CELL PLANTINGS

The cells used in the "mixed cell" plantings were sometimes fuseaux and sometimes aleuries. Fuseaux are fusiform, multicellular, septate spores, each segment of which may sprout. These were designated as macroconidia in the recent paper of Emmons [17] bearing on *Achorion*

gypseum. Both gross and microscopic cultures were made from these polyspore plantings.

Trichophyton interdigitale (no. 1043).—Of the four gross cultures, each planted with two aleuries, two grew into typical colonies and two died.

Microsporum fulvum (no. 1316).—Six cultures were made on dextrose agar from single fuseaux, which are produced by this particular species in great abundance on artificial mediums. They looked exactly like the solitary aleurie culture that matured. This was also true for *Achorion gypseum*.[17] Our cultures from single fuseaux differed from the control in that they were white in the early stages, not assuming the typical café au lait and powdery appearance until they were quite old, and also in that they had suggestions of radial furrows.

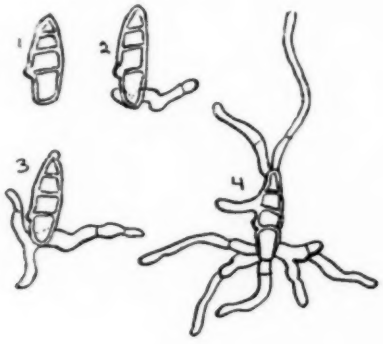

Fig. 2.—Drawing illustrating the multicellular considerations involved in fuseaux (Microsporon fulvum no. 1316). The multiplicity of strains obtainable from a single structure is illustrated in the forty-two hour stage: *1*, the fuseau at planting; *2*, eighteen hours later; *3*, twenty-four hours after planting; *4*, forty-two hours after planting.

Hanging-drop cultures made from two aleuries of *Trichophyton interdigitale* (no. 1043) and *Trichophyton granulosum* (no. 2032), differed in no way from the monospore cultures. Of the eighteen hanging-drop cultures made from *Microsporum fulvum*, fourteen were from fuseaux and four from single aleuries. The latter are mentioned here because they serve as controls in this particular set of tests; the results are recorded in table 2. Only five fuseaux and three aleurie cultures matured. The remaining nine from single fuseaux and one from an aleurie never developed completely, even though they sprouted. In the case of *Microsporum fulvum* the same characteristics as were produced with one fuseau or one aleurie were obtained each time in hanging-drop cultures—first, with an aleurie and a fuseau; second, with two fuseaux, and third, with two fuseaux and four aleuries.

MORPHOLOGY IN THE SECOND GENERATION

It was necessary to inquire into the second generation because the possibility still remained that pleomorphism might exist, more or less latent, even in pure line cultures, and might lead to erroneous conclusions when reading the cross plantings.

(1) *Subcultures from Single Cell Gross and Hanging-Drop Cultures: Trichophyton interdigitale* (no. 1043).—No new characteristics developed either on the dextrose agar slants or in giant flask cultures made from both gross and hanging-drop pure line cultures.

Trichophyton interdigitale (no. 1894).—The ten subcultures made from single cell strains on dextrose agar were not strictly true to form in that some were highly pleomorphic while others, which retained the original yellow powderiness, had deep craters in the centers. Cultures made from two of the single cell hanging-drops were exactly like the originals.

Trichophyton purpureum (no. 1550).—In the same way, subcultures of *T. purpureum* on dextrose agar slants made from ten gross cultures of single cells, and from two hanging-drop cultures of this strain were not different from the original ones.

These tests showed that pleomorphic tendencies were present early in one of the strains (no. 1894), but not in the other two, even in pure line material. They indicated that readings on the cross plantings of no. 1043 and no. 1550 could be made without reservations, but had to be qualified in no. 1894. They showed that for no. 1894 such pleomorphism was inherent and not contingent on the conditions involved in cross planting.

(2) *Subculture from "Mixed Cell" (Fuseau) Plantings: Microsporon fulvum* (no. 1316).—The three dextrose agar cultures made from a mature hanging-drop culture of *Microsporon fulvum* showed marked radial furrows that the control did not have. Had these fuseaux been single cells, this would bring "furrowing" into consideration as a pure line characteristic; but since they were not, the results do not bear on the single cell phases of these studies. They do, however, complicate the problem for *Microsporon fulvum* and make it necessary to inquire most critically into the genetic structure of the different cells of a fuseau. This is quite beyond the scope of this paper.

MORTALITY IN SINGLE CELL PLANTINGS

Besides showing the numbers of cultures secured from tests for heterothallism, tables 1 and 2 indicate that every aleurie did not have sufficient "vitality" to continue growth after the first sprouting.

This is not a new experience in biology. Churchman,[24] in connection with his work with *Bacillus coli* which was nonsusceptible to gentian violet on medium containing the dye, met discrepancies in the growth response of different bacterial cells. Growth, which was delayed, was secured in only two of a whole series of single cell transplants; "moreover, transplants of small groups of organisms (5-15) did not grow, though transplants of thirty individuals grew very regularly." Churchman said that the explanation of this phenomenon was not purely quantitative, for "thirty cells accomplish more than thirty times what one cell can accomplish." Although gentian violet did not enter into the work with these dermatophytic cells, a similar absence of "communal activity" may have been responsible for the mortality under discussion. Gee and Hunt,[25] in working with bacteria, reported "one to five successful growths from ten transfers of single cells from the same suspension," while Duff [26] obtained from five to eight positive bacterial cultures out of ten.

Considering next the nonmedical species of fungi, the percentage of spores of neurospora that germinated was reported by Dodge [3] as being "ordinarily high when the spores have been properly heated." For the agaricaceae, Sass [27] gave the percentage of spore germination as variable from 5 to 95 per cent. Of 200 isolations, 149 mycelia grew and 42 died soon after germination. Styer [28] found that "the spores of *Agaricus campestris* germinate more quickly in masses than when separated."

The percentage of positive cultures secured from single conidia in this work (tables 1 and 2) compare favorably with the results that have been recorded by others for bacteria and fungi, although it is recognized that the conditions in the latter experiments did not exactly parallel those in this work. The cause of the mortality cannot be definitely stated. As a small piece of the surrounding medium was always carried along, and the young colony was undisturbed, it probably was not killed by mishandling. While it is possible that the reason for the mortality may belong in the category of "communal activity," this is only a phrase and not an explanation. It is more probable that it comes under the law of "percentage of survival" of germinated seeds, which is so widely recognized by the botanist.

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25. Gee, A. H., and Hunt, G. A.: Single Cell Technic, J. Bact. **16**:327 (Nov.) 1928.

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27. Sass, J. E.: The Cytological Basis for Homothallism and Heterothallism in the Agaricaceae, Am. J. Botany **16**:663 (Nov.) 1929.

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TESTS FOR HETEROTHALLISM

The meaning of heterothallism has been indicated in previous paragraphs. Its expression thus far has been confined to the development of sexual reproductive bodies, although Weidman [1] indicated theoretical possibilities, as for example, physiologic variations such as pathogenicity. So far as the work and the material herewith are concerned, there are several items which theoretically are subject to variation that should not be overlooked as criteria for judging heterothallism. The conditions that have been systematically inquired into in our cross plantings are as follows:

Gross.—The rate and mode of growth, the volume of colony, texture, configuration of the surface, color, pigmentary effects on the medium and invasion of the substrate comprises the gross characteristics.

Microscopic.—The microscopic characteristics involve essentially the development of asci or other special reproductive bodies (histologic sections of agar colonies). This phase, to be exhaustive, should extend into the employment of cross plantings in hanging-drop preparations and inquiries as to changes not alone in the development of asci there, but of other, even nonsexual reproductive bodies. It is planned to cover the former in future studies, but as to the latter, the observations reported in a previous paper (Spring [2]) would discourage trials because the organes are so inconstant. Additional microscopic characteristics to be studied as responsible for heterothallism cannot be given in detail here because it would involve too much technical description. In general, judgment of heterothallism would have to be based on (1) a full knowledge of the scope and limitations of microscopic changes for each species; (2) thereafter on an estimate as to whether the cross planting departed from the standard; and if so (3) to what extent, and (4) in what particular respect.

All of the foregoing considerations have been kept in mind when reading and analyzing criteria in the cross plantings; it would be tiresome to refer to each specifically in the results to be recorded hereafter.

TECHNIC OF "CROSS" PLANTING

This differed from the conventional mycologic technic only in that two pieces of inoculum from different pure line strains were laid on the agar slant, so closely that they almost touched. Dextrose agar was used in all cases.

It will be observed that in the major work, ten pure line strains were available in two different series of *Trichophyton interdigitale* and one of *Trichophyton purpureum*. The ten were crossed in all possible combinations, the resultant colonies were analyzed and the attempt was made to group changes or differences so as to interpret them finally into terms of heterothallism.

Trichophyton interdigitale (no. 1043).—In the preliminary work "giant" flask cultures were employed as well as agar slants; characteristics may develop in

"giant" cultures that may not appear to advantage in the more cramped environment of the test tube. At a time when only four pure line strains were available, they were subcultured separately and also crossed in all possible combinations in both the flask and the test tube cultures. The resultant colonies showed no new or unusual characteristics.

In addition, ten single cell strains, all isolated at the same time and of the first or second generation, carried on conservation medium, were crossed with each other in all possible combinations. Controls were also made from each, thus

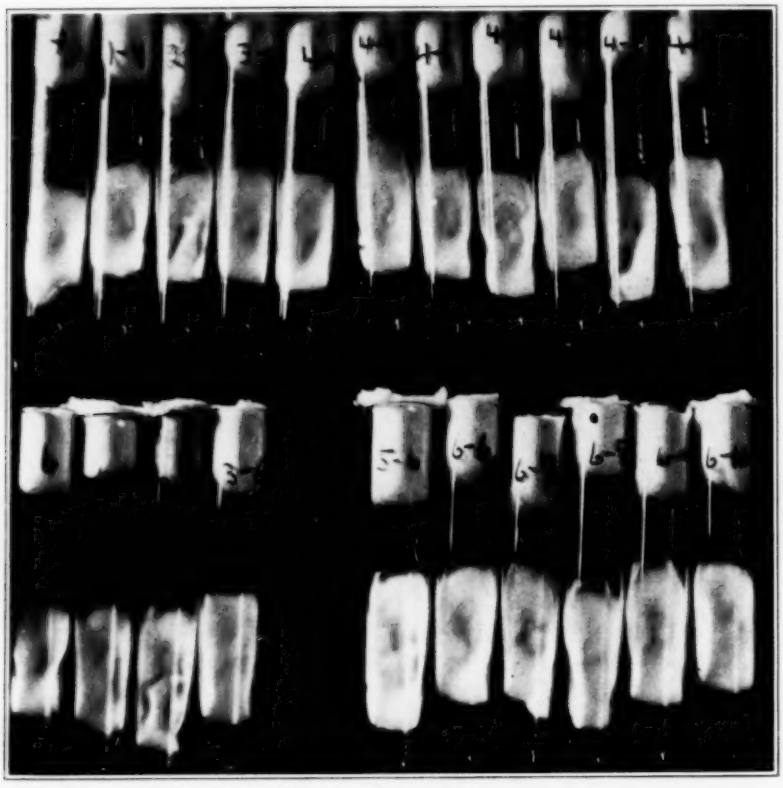

Fig. 3.—Cross plantings of pure line strains; no. 4 on the top row, no. 6 on the bottom row. The colonies in each tube at the extreme left have not been crossed (controls). These cultures illustrate what was regarded as a smooth variety (dissociant?) of Trichophyton interdigitale (no. 1043). The colonies were fourteen days old. The test tubes measured 1 by 6 inches, from which the size of the colony may be computed.

making a total of sixty-five cultures. The controls consisted of a single and a double planting of the same pure line strain; in the latter the explants were taken from different portions of the same colony.

In the younger stages, all of the resulting colonies closely resembled each other in that they were white and rather fluffy. At the end of ten days they were, on the whole, more loosely duvetuse and showed differences. Some were

umbonate and others slightly depressed and becoming folded in the center. At the end of two weeks it was possible to divide them definitely into smooth and folded colonies (figs. 3 and 4). The smooth colonies were replicas of the mother pure line strains; the folded ones were different only in point of surface conformation. On comparison with the controls of these groups, the following results were recorded:

1. Matings of "smooth" haplonts with each other and with themselves yielded "smooth" colonies without exception. Haplonts 4, 6, 8 and 10 belonged in this group.

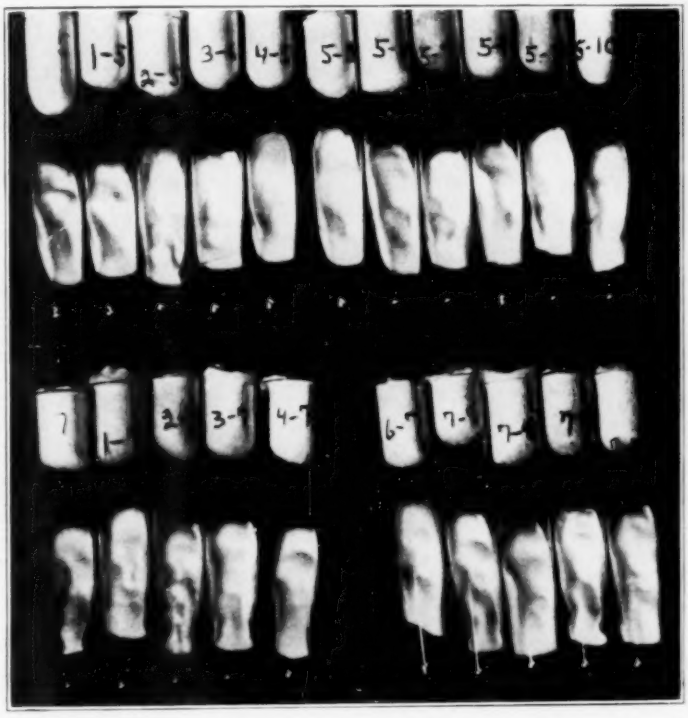

Fig. 4.—Cross plantings under the same conditions as in figure 3, but illustrating the colonies classified as "wrinkled." Colonies of Trichophyton interdigitale (no. 1043) 14 days old.

2. Furthermore, there seemed to be a factor of dominance in the smooth colonies as matings of smooth colonies with certain folded ones also yielded smooth colonies.

3. As exceptions to this general "dominance" on the part of smooth colonies, three of the "folded" strains persisted in exhibiting folds even in the cross plantings, namely, strains 2, 7 and 9.

4. "Folded" cross plantings developed from strains 1, 2, 3, 5, 7 and 9.

Trichophyton interdigitale (no. 1894).—Ten cultures from single cells were also employed in testing this strain. They were of the characteristic type and closely resembled each other. They were likewise crossed as described for the

preceding series. In the early stages, the controls and cross plantings showed similar growth: white at first, later becoming flattened and powdery yellow in the center. It will be recalled that pleomorphism was found to be present in a previous set of tests described under "morphology in the second generation."

At the end of twenty-two days, however, it was possible to divide them into three definite groups as follows: (1) those in which the yellow powderiness persisted. These colonies had deep craters in the centers and showed typical brown

Fig. 5.—Cross plantings of pure line cultures of Trichophyton interdigitale (no. 1894) 3 weeks old. The upper row shows a pleomorphic strain (no. 1) which overgrew even the nonpleomorphic strains. The lower row consists of nonpleomorphic strains. There are no distinctive features to indicate heterothallism.

pigmentation on the under surface diffusing into the medium (strains 6, 8, 9 and 10); (2) the intermediates in which the attempts at crater formation and powderiness were nearly overgrown with a white pleomorphic duvet; these were pale on the reverse side (strains 2, 3 and 4); and (3) those that were composed entirely of white pleomorphic growth (strains 1, 5 and 7).

Consistent results occurred in the cross plantings of crater-crater and pleomorphic-pleomorphic strains (fig. 5) except in the case of $2 + 2$, which failed to show the crater. With this exception, groups 1 and 3 bred true; that is,

crater-crater crossings yielded only crater colonies, and pleomorphic-pleomorphic, only pleomorphic colonies. This gives encouragement for the continuance of studies of heterothallism. The cross planting of 6 + 9 was the most pigmented and most powdery; it exhibited the deepest crater and, in theory, might be regarded as typical of the crater-forming cross plantings.

Paraffin sections of both crater and pleomorphic colonies were made to determine whether any changes had taken place in the depths of the colonies that could not be observed in "in toto" preparations and that might be pointing toward heterothallism. Asci were looked for particularly. No differences could be determined; the same organes and the same arrangements in strata were found in both sets of colonies.

Trichophyton purpureum (no. 1550).—Ten single cell strains of this organism were likewise crossed. All of the resultant colonies were strikingly alike. They were composed of a white flattened duvet, cream-colored in the center, with a barely recognizable yellowish cast at the upper portion of the slant. The yellowish cast was not consistently present in given single cell strains, and could not be referred to organized genetics. It probably depended on differences in the content of moisture in the substratum in this unstable portion of agar slants. Controls and cross plantings showed a definite pink coloration at the margin between the medium and the wall of the tube; this was the well known purplish-red of *Trichophyton purpureum.*

As in the case of *Trichophyton interdigitale* previously described, microscopic examinations of sections of pure line strains and cross plantings did not reveal any differences, either as to individual elements (organes) or arrangements into strata or otherwise.

Microsporon fulvum (no. 1316).—Incidentally, cross plantings of colonies of single fuseaux furnished no new characteristics. Of course, no deductions in heterothallism could be made from these tests because the materials were not of pure line.

SUMMARY AND CONCLUSIONS

1. The occurrence of heterothallism in the pathogenic fungi of man and other animals deserves study, both morphologically and physiologically. If established, it would have taxonomic (determinative) and pathogenic significance.

2. Monospore technic with these fungus cells is not difficult; it is practical with the equipment of the ordinary bacteriologic laboratory.

3. In the three strains of two species tested, *Trichophyton interdigitale* and *Trichophyton purpureum,* heterothallism could not be distinguished with finality. There were differences in the surface configuration of one strain of *Trichophyton interdigitale,* and in the pleomorphism as well as surface of a second strain. However, in the presence of pleomorphism a significance in the direction of heterothallism cannot be assigned to these phenomena unless it is first demonstrated that pleomorphism itself can be a heterothallic expression.

4. Incidentally, it was found that the same kind of a colony developed from such highly specialized structures as fuseaux, as developed from less specialized ones like aleuries. Also that, as is to be expected, the same results were obtained from two aleuries as from one.

5. With our human dermatophytes we have had an experience similar to that of other workers in single cell technic: a large proportion of aleuries and fuseaux, approximately 50 per cent, failed to develop to maturity, even after a preliminary sprouting.

6. It appears that the viable aleuries in a species increase in direct proportion to the degree of powderiness of the colony, as seen grossly (five species tested). This corresponds roughly to the clinical symptoms, the more granular species such as *Trichophyton granulosum* inducing the more severe clinical lesions. The granular type of *Trichophyton interdigitale* (1894), which was obtained from a more severe lesion than the nonpowdery type, yielded a higher percentage of single cell "takes" on culture medium.

ANGIOKERATOMA

COMPREHENSIVE STUDY OF THE LITERATURE AND REPORT OF A CASE *

EUGENE F. TRAUB, M.D.
AND
JESSE A. TOLMACH, M.D.
NEW YORK

Recently we observed a typical case of angiokeratoma Mibelli, and since the condition is uncommon we record this case. Judging from the number and types of cases that have been reported in the literature as angiokeratoma, much confusion exists as to the true nature of this disease. A thorough study of practically every case reported [1] revealed that the typical cases of the disease, as classified and described by the accepted authority, Mibelli, are comparatively few, and that a number of cases reported as angiokeratoma bear a clinical resemblance to the classic case, but are really a different entity. Therefore, we have undertaken the task of clarifying the literature on this subject by sifting out of the melée the true cases of the condition according to Mibelli's description and separating them from the ones that do not belong to the group.

Briefly, according to Mibelli's report in 1889, angiokeratoma is a disease of the skin of the bony protuberances of the extremities, characterized by dark red and purplish spots varying in size from that of a pinpoint to that of a pinhead; these spots are discrete or aggregate and sometimes confluent. They are rough, hard and warty, and usually bleed freely when pricked with a needle. The clinical factors that establish the diagnosis are the usual location, on the hands and feet, and sometimes on the knees and elbows; a history of pernio, indicating a disorder of the blood vessels and peripheral asphyxiation, and the onset of the lesions at an early age. Histologically, Mibelli pointed out dilated blood spaces in the epidermis and papillary bodies and dilated spaces and blood vessels throughout the corium. He also demonstrated the presence of marked perivascular infiltration of leukocytic cells. Subse-

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1. Every reference to the subject of angiokeratoma available at the library of the New York Academy of Medicine was studied. Whether this would include every case ever reported, we cannot say. We believe, however, that the list of cases obtained is practically complete.

quently Sutton pointed out the fragmentation and breaking up of elastin surrounding the walls of the blood vessels.

This condition remained a fairly well defined clinical and histologic entity, Mibelli's description having been generally accepted as authentic until 1896, when Fordyce reported an atypical case of angiokeratoma. In this instance the location of the lesions on the scrotum instead of on the extremities, the advanced age of the patient and the absence of pernio were atypical, but the histologic and clinical appearances were apparently identical with those in Mibelli's case. Following this report, a number of cases of angiokeratoma of the scrotum and of other atypical locations were reported, in which the histologic structure simulated that of the true Mibelli type. Some authors contended that these scrotal cases were not true angiokeratomas because of their digression from the classic picture in three major points, namely: the age of the patient, the location of the lesions and the absence of a history of pernio. However, we feel that as these cases are reported as having shown a true histologic picture of the Mibelli type and that as Mibelli's nomenclature, "angiokeratoma," designates only the pathologic anatomy, namely, a disease of the blood vessels together with hyperkeratosis, these cases are rightfully diagnosed as angiokeratoma. But, since in the one instance the condition follows an alteration of the blood vessels in pernio, and in the other there is no history of pernio but perhaps a congenital weakness of the walls of the blood vessels with the formation of phlebectaces, the difference in etiology should be indicated in the diagnosis; namely, the former condition should be called "angiokeratoma Mibelli" and the latter, "angiokeratoma without pernio (Fordyce)." It is possible that biochemically the conditions may be entirely different, but with our limited knowledge of the pathology, we are unable at present to prove any essential difference in the two types.

On the other hand, after the publication of the first report of an atypical case of angiokeratoma, many cases have been reported as angiokeratoma of the scrotum and of other atypical locations, with atypical histories, but without a confirming histologic report. The diagnosis was entirely clinical, and, in truth, many of these cases undoubtedly were atypical senile angiomas, verrucose angiomas, vascular nevi, nevoid and telangiectatic growths, lymphangiomas, verrucae vulgaris or even lupus vulgaris. In some cases, such as that reported by Matsumato, the histologic examination showed angioma and keratosis, and they were therefore reported as angiokeratoma. But angioma plus keratosis does not constitute angiokeratoma Mibelli, for angiokeratoma Mibelli is not an angioma; the term is misleading. As was stated, the condition is merely an alteration in the blood vessels, associated with hyperkeratosis of the epidermis.

REVIEW OF THE LITERATURE

Although the name of angiokeratoma as applied to this condition dates from Mibelli, the disease was described before by several authors.

In 1862, Bazin,[2] under the name "naevus a pernione," made reference to a disease that usually occurred on the hands and feet and the face following pernio.

In 1877, Cottle [3] reported six cases of warty growths, one of which, from his description, was a clinically typical angiokeratoma. It was the case of a woman, aged 21, who gave a history of pernio and who showed an eruption on the hands, consisting of discrete and aggregated red spots, which were prone to bleed. The other cases that he described in the same report were merely warty growths, and not angiokeratoma Mibelli.

In 1881, Breda [4] described a disease of the hands and feet, under the name "dermatite de congelazione," consisting of blood red dots of a warty nature, which was apparently the same as Mibelli's disease.

In 1886, Secheyron [5] described a case of verrucose nevi following pernio, "a variety of naevus pernione of Bazin." It was the case of a patient who, until the age of 18, suffered from pernio during the winter and in whom violaceous spots developed on the fingers and toes. A section of some of the lesions showed thickening of the epidermis, papillary spaces and globules of blood in the level of the vascular openings.

In 1887, Colcott Fox [6] reported the case of a girl, aged 9 years and 9 months, who gave a history of pernio and showed typical spots on the dorsal surface of the hands and feet, which were swollen and puffy. He described the condition as being similar to a disease known then as lupus lymphaticus, and believed it to be due to a lymphatic disorder. Other members of this patient's family were similarly affected.

Radcliffe Crocker,[7] in 1888, in his textbook, gave a description of the disease under the name of verruca. In 1891,[8] after Mibelli's report appeared, Crocker reported his case in the literature. It was a typical eruption on the typical sites on the fingers and knuckles of a girl, aged 17, who had had pernio for a number of years.

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2. Bazin: Affections cutanées artificielles (naevus a pernione), Paris, A. Delahaye, 1862.

3. Cottle: St. George's Hosp. Rep. **60**:758, 1877-1878.

4. Breda: Gior. ital. d. mal. ven. **16**:159, 1881; quoted by Joseph: Dermat. Ztschr. **1**:16, 1893-1894.

5. Secheyron: Arch. gén. de méd. **3**:418, 1886.

6. Fox, Colcott: Westminster Hosp. Rep. **3**:125, 1887.

7. Crocker, Radcliffe: Diseases of Skin, ed. 1, Philadelphia, P. Blakiston's Son & Company, 1888, p. 512.

8. Crocker, Radcliffe: Brit. J. Dermat. **3**:342, 1891.

TABLE 1.—*Unquestionable Typical Cases of Angiokeratoma*

Author	Year	Patient	Age	History	Location	Histopathology	Comment
Pringle: Brit. J. Dermat. **2**: 209.....	1891	Female	24	Pernio	Hands and feet	Typical	
Pringle: Brit. J. Dermat. **2**: 209.....	1891	Female	21	Pernio	Hands and feet	Typical	
Pringle: Monatschr. f. prakt. Dermat. **13**: 11	1891	Female	..	Pernio	Lobe of ear	None given	Considering Pringle's extensive and creditable work on the subject of angiokeratoma, we are inclined to believe that this case is typical angiokeratoma on an unusual location; it becomes a question whether or not Mibelli, in considering extremities, would have included the ears, which were subject to frostbite, as were the hands and feet; it is surprising that with so frequent an occurrence as frostbite of the ears, more cases of the eruption on this site have not been noted.
Deydier and Audry: Lyon méd. **70**: 323...	1892	Male	23	Pernio	Dorsa of hands	None given	Eruption first appeared after typhoid
Brocq: Ann. de dermat. et syph. **3**: 819....	1892	Male	17	Pernio	Hands	None given	
Thibierge: Ann. de dermat. et syph. **3**: 1139	1892	Male	30	Pernio	Hands	None given	
Joseph: Dermat. Ztschr. **1**: 16 (Frey, in Vogt, Berlin Dissertation)	1893	Male	19	Pernio	Hands and feet	Typical	
Frey: ibid.	1893	Male	17	Pernio	Hands and feet	Typical	
Frey: ibid.	1893	Female	20	Pernio	Hands and feet	Typical	
Frey: ibid.	1893	Male	21	Pernio	Hands and feet	Typical	
Frey: ibid.	1893	Male	28	Pernio	Hands and feet	Typical	
Frey: ibid.	1893	Female	24	Pernio	Hands and feet	Typical	The patients in this case and the preceding one were brother and sister
Dubreuilh: Ann. de dermat. et syph. **4**: 379	1893	Female	50	Pernio	Both hands	Typical	
Escande: Thèse de Toulouse.....	1893	Male	25	Pernio	Hands and feet	Typical	Patient had tuberculosis
Audry: Ann. de dermat. et syph. **4**: 381... (3 cases)	1893	Male	15	Pernio	Hands and feet	None given	Patient had tuberculosis and syphilis
		Male	22	Pernio	Hands and feet	None given	
		Male	21	Pernio	Hands and feet	None given	
Gebert: Monatschr. f. prakt. Dermat. **22**: 517	1896	Male	12	Pernio	Fingers and toes	Typical	
Isaac: Monatschr. f. prakt. Dermat. **25**: 621	1897	Female	15	Pernio	Fingers and hands	Typical	
Leredde and Haury: Bull. Soc. franç. de dermat. et syph. **10**: 177	1898	Male	15	Pernio	Hands and feet	Typical	Coincidental with tuberculosis; patient also had some lesions on the scrotum, but they showed no hyperkeratosis
Wisniewski: Arch. f. Dermat. u. Syph. **45**: 357	1898	Male	16	Pernio	Hands	None given	
Truffi: Gior. ital. d. mal. ven. **37**: 712.....	1902	Male	24	Pernio	Hands and feet	Typical	Angina pectoris and arteriosclerosis developed
Leredde and Pautrier: Bull. Soc. franç de dermat. et syph. **13**: 35	1902	Female	22	Pernio	Hands	None given	Patient had lupus pernio of the nose, and there was tuberculosis in the family
Dorè: Brit. J. Dermat. **25**: 323.....	1903	Female	18	Pernio	Hands and feet	None given	

Pautrier: Arch. f. Dermat. **69**: 145; **71**: 572	1904	Female	22	Pernio	Hands and feet	Typical	Patient was cyanotic; there was tuberculosis in the family; patient also showed lupus pernio of the nose
de Beurmann and Gougerot: Ann. de dermat. et syph. **6**: 875	1905	Female	20	Pernio	Hands and feet	Typical	Patient showed attenuated tuberculosis
Rau: Monatschr. f. prakt. Dermat. **4**: 439	1905	Male	22	Pernio	Hands and feet	Typical	
Grouven: Verhandl. f. deutsch. Dermat. Gesellsch., IX Kongress, p. 327	1906	.....	22	Pernio	Left arm, shoulder and left breast	Typical	Although in this case the location was atypical, everything else, including the histology, was indicative of angiokeratoma and, as in Pringle's case on the lobe of the ear, we feel that this belongs in the typical group
Frohwein: Monatschr. f. prakt. Dermat. **42**: 345	1906	Female	17	Pernio	Hands, feet, elbows and knees	Typical	
Mucha: Arch. f. Dermat. u. Syph. **96**: 342	1909	Male	13	Pernio	Feet	Typical	Sister had similar eruption; father had pernio
Scheuer: Arch. f. Dermat. u. Syph. **98**: 251	1909	Female	21	Pernio	Hands and feet	Typical	
Scheuer: ibid.	1909	Female	..	Pernio	Hands and feet	Typical	
Scheuer: ibid.	1909	Female	..	Pernio	Hands and feet	Typical	This patient and the preceding one were sisters; two brothers had pernio
Brandweiner: Wien. med. Wchnschr. **19**: 1263	1912	Male	18	Pernio	Toes	Typical	Patient had tuberculosis
Pringle: Proc. Roy. Soc. Med. (Sect. Dermat.) **6**: 76	1913	Male	46	Pernio	Hands and feet	Typical	This and the following three cases occurred in one family, father and three sons
Pringle: ibid.	1913	Male	17	Pernio	Hands and feet	Typical	Father and the two oldest sons had tuberculosis of the lungs or the joints
Pringle: ibid.	1913	Male	13	Pernio	Hands and feet	Typical	
Pringle: ibid.	1913	Male	8	Pernio	Hands and feet	Typical	
Sibley: Proc. Roy. Soc. Med. (Sect. Dermat.) **9**: 121	1915	Female	12	Pernio	Hands and feet	Typical	
Senear: J. Cutan. Dis. **35**: 842.....	1917	Female	29	Pernio	Toes and fingers	None given	
Harris: J. Cutan. Dis. **35**: 849.....	1917	Female	21	Pernio	Toes and fingers	None given	
Pusey: J. Cutan. Dis. **37**: 274.....	1919	Female	29	Pernio	Toes and fingers	None given	
Leri, Tzanck and Peron: Bull. Soc. franç de dermat. et syph. **30**: 353	1923	Female	18	Pernio	Hands	None given	Patient showed adenopathy of the left cervical region
Queyrat: Bull. Soc. franç de dermat. et syph. **30**: 327	1923	Male	18	Pernio	Hands and feet	Typical	
Wertheim: Arch. f. Dermat. u. Syph. **147**: 433	1924	Male	28	Pernio	Fingers	Typical	
Tomasone: Riforma med. **40**: 1057.....	1924	Male	..	Pernio	Hands and feet	Typical	Patient had tuberculosis
Hudelo, Caillaud and Chabrun: Bull. Soc. franç. de dermat. et syph. **32**: 208	1925	Female	13	Pernio	Hands and feet	Typical	Patient had tuberculosis
Goldschlag: Dermat. Wchnschr. **80**: 321...	1925	Female	15	Pernio	Hands and feet	Typical	
Chargin: Arch. Dermat. & Syph. **15**: 489 (April)	1927	.....	20	Pernio	Hands and feet	None given	
Wile and Belote: Arch. Dermat. & Syph. **18**: 503 (Oct.)	1928	Male	25	Pernio	Hands and feet elbows and knees	Typical	

In 1889, another case was reported by M. Merklen,[9] which he called "telangiectasis following chilblains."

In January, 1889, Dubreuilh [10] reported a condition under the name of telangiectatic warts, but it was evidently angiokeratoma Mibelli. It was the case of a girl, aged 19, who showed lesions on the fingers and on the ulnar margin of both hands, and who gave a history of pernio.

In the same year, Colcott Fox [11] reported two more cases under the title of "Cases of Lymphangiectasis of the Hands and Feet in Children," which, after Mibelli's report was published, he admitted were typical angiokeratomas. One of his cases was that of a girl, aged 12, who suffered from pernio and showed tiny purplish, warty elevations on the toes; the second case was that of a boy, aged 9, with a history of pernio, who presented the condition on the fingers and toes.

In spite of all of these observations of the disease, it remained for Mibelli, in 1889 [12] and 1891,[13] to make a definite place for it among the dermatologic entities, by a precise classification based on the microscopic picture, the clinical aspects, the etiology and the location, and he gave it the name angiokeratoma, which characterized its pathologic anatomy. Since Mibelli's work the unquestionably typical cases enumerated in table 1 have been reported. Most of them agree in all points of location, history and clinical and histologic appearance. A few reporters do not give a histologic study, but from their descriptions, and in the opinion of other physicians, the growths were without doubt true angiokeratomas (table 1).

Table 2 gives a list of the reported cases that are similar to Mibelli's in histologic and clinical appearance, but that differ from the usual angiokeratoma in location, the absence of a history of pernio and the late age of the onset; therefore, they are tabulated separately under the designation of "angiokeratoma without pernio (Fordyce)."

In table 3 are listed the rest of the cases reported either as angiokeratoma or as atypical angiokeratoma, but which in our opinion digress so far in several or all essential factors from the classic picture that it only leads to confusion to associate them with the name of angiokeratoma. We include in this table those cases that bear some slight clinical resemblance to true angiokeratoma, but that show a different histologic picture, or the authors of which fail to give a histologic study to confirm or negate a questionable diagnosis. We feel that these cases should be definitely excluded from the classification of angiokeratoma.

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9. Merklen, M.: Catalogue des moulages caloriés du musée de l'hôpital St. Louis, 1889.

10. Dubreuilh: Ann. de la policlin. de Bordeaux **1**:50 (Jan.) 1889.

11. Fox, Colcott: Illust. M. News **4**:71 (July 27) 1889.

12. Mibelli: Gior. ital. d. mal. ven. **24**:285, 1889.

13. Mibelli: Gior. ital. d. mal. ven. **26**:159, 1891.

TABLE 2.—*Cases of Angiokeratoma Without Pernio*

Author	Year	Patient	Age	Location	History	Histopathology	Comment
Zeisler: Tr. Am. Dermat. A. **17**: 54.....	1893	Male	53	Hands and feet	No pernio	Typical	This was the first case reported in America; the patient showed nevus-like patches and pedunculated vascular tumors on forearms, legs, thighs and auricles; although there was no history of chilblains, the patient's occupation as butcher exposed his hands and feet to extreme cold
Moure: Rev. de laryng. **13**: 913.....	1894	Female	25	Right vocal cord	No pernio; followed influenza	Typical	Patient had sarcomatous lesion on the right hand; husband died of tuberculosis
Fordyce: J. Cutan. Dis. **14**: 81.....	1896	Male	60	Scrotum	No pernio; double varicocele	Typical	
Leredde and Milian: Ann. de dermat. et syph. **9**: 1095	1898	Female	19	Toes, feet and legs	No pernio	Typical	Patient had showed adenopathy since infancy; M. Tennenson diagnosed the condition as angiokeratoma Mibelli, and the author claimed that while the histology was typical of Mibelli's case, it was also similar to that of "tuberculid necrotiques"
Wisniewski: Arch. f. Dermat. u. Syph. **45**: 357	1898	Female	23	Hands and feet	No pernio	Typical	This case was regarded as typical by other authors
Buschke: Monatschr. f. Dermat. **35**: 357	1902	Male	58	Scrotum	No pernio	Typical	Patient also showed prurigo Hebra
Sutton: J. A. M. A. **56**: 189 (July 15)...	1911	Male	64	Scrotum and right eyeball	No pernio	Typical	Biopsy of the tumor of the eyeball as well as of eleven tumors of the scrotum was made, and the histology was similar to that of Mibelli's case
Planner: Wien. med. Wchnschr. **63**: 2425	1913	.....	15	Thigh and instep	No pernio	Typical	Patient showed tendency to elephantiasis; at first the author diagnosed the case as nevus pigmentosus, but the histology showed features similar to Mibelli's case
Stumpke: Arch. f. Dermat. u. Syph. **121**: 291	1915	Male	28	Crural region; scrotum; generalized spots	No pernio; had rheumatism of joints	Typical	
Weicksel: Deutsche med. Wchnschr. **51**: 898	1925	Male	22	Arms, breasts, thighs and back	No pernio	Typical	
Weicksel: ibid.	1925	Male	18	Abdomen, back, scrotum and genitals	No pernio	Typical	In this and the preceding case, the patients were brothers; the patient showed a tendency to tuberculosis; clinically, the eruption resembled purpura hemorrhagica, but histologically, the picture was that of angiokeratoma Mibelli

TABLE 3.—*Cases Excluded from Classification of Angiokeratoma*

Author	Year	Patient	Age	Location	History	Histopathology	Comment
Renault: Ann. de dermat. et syph. **5**: 1248	1894	.....	20	Corners of month; buccal mucosa	No pernio; no blood vessel disorder	None given	This case was presented as lymphatic varicosities of the buccal mucosa by Tenneson and Darier
Eddowes: Brit. J. Dermat. **7**: 265.....	1895	.....	50	Right leg	No pernio	None given	This case was keratosis over the course of varicose veins of the leg
Anderson: Brit. J. Dermat. **42**: 113.....	1898	Male	39	Trunk, limbs and genitals	No pernio	No evidence of disease of blood vessels; no keratosis	Atypical in every respect
Hallopeau and Trastour: Ann. de dermat. et syph. **11**: 632	1900	.....	3	Dorsum of right foot	Pernio	Hyperkeratosis and acanthosis	Pathology distinctly dissimilar
Mantaux: Ann. de dermat. et syph. **14**: 15	1903	.....	22	Palms and soles	Pernio	Porokeratosis	According to Matsumato, the diagnosis should have been "porokeratosis papillomatous palmare et plantare"
Malinowski: Monatschr. f. prakt. Dermat. **45**: 439	1907	.....	20	Right upper extremity; left arm	No pernio	Shows blood-filled spaces in papillary layer	Author called case punctiform angiomas simulating angiokeratoma, but angiokeratoma is not an angioma
Pospélow: Ikonographia Dermatologia **13**: 63	1907	.....	11	Left foot	Pernio	None given	Congenital vascular nevus in which keratosis developed
Sasakowa: Japan. Ztschr. f. Dermat. u. Urol. **8**: 597	1908	.....	..	Right lower extremity	Pernio	Hyperkeratosis; angioma	Lesion was angioma
Judin: Dermat. Ztschr. **15**: 36.....	1908	Male	23	First and second fingers of left hand	Pernio	Suggestive of anomalous case of angioma	Resembled angioma histologically and clinically, and therefore, despite the history of pernio, the diagnosis of angiokeratoma should be excluded
Beck: Monatschr. f. prakt. Dermat. **49**: 349	1909	Male	66	Dorsa of hands and flexor surface of carpal region; right upper arm	No pernio; rheumatic pains of extremities	None given	Author stated that his case was clinically typical of Mibelli's case, but gave no pathologic observations to prove this, and the atypical location and absence of pernio are against the diagnosis of angiokeratoma
Sequeira: Proc. Roy. Soc. Med. (Sect. Dermat.) **4**: 28	1910	Male	21	Hands, elbows, knees, feet, ears and wrists	No pernio; low peripheral circulation	Atypical	Pringle expressed the belief that this was not angiokeratoma, but rather an instance of tuberculosis occurring in a person with low peripheral circulation; the author called the condition angiomatous
Williams: Proc. Roy. Soc. Med. (Sect. Dermat.) **4**: 95	1910	Female	17	Little finger of one hand; small papule	No pernio	Showed lupus-like tissue	Histology indicated lupus vulgaris
Trowbridge: J. A. M. A. **58**: 1130 (Sept. 30)	1911	Male	61	Scrotum and testes	Vague history of pernio	None given	No histologic study to confirm diagnosis
Sutton: J. A. M. A. **57**: 189 (July 15)...	1911	Male	61	Scrotum	No pernio; dilated venules	None given	Atypical in all respects and no pathology to confirm the diagnosis
Kyrle: Arch. f. Dermat. u. Syph. **112**: 11	1911	.....	15	Right thigh, leg and back of foot	No pernio	Angiomatous	Pathologic examination shows angioma
Azúa: Tr. d. Soc. españ. de dermat. y sif., in Arch. f. Dermat. u. Syph. **112**: 888	1912	.....	..	Hands and feet	No pernio; showed scleroderma	None given	In absence of histologic study, the facts are insufficient to establish a diagnosis of angiokeratoma
Bettman: Verhandl. d. deutsche dermat. Gesellsch. X. Kongress, p. 377	1908	.....	..	Right arm, chest and back	No pernio	Angiomatous	Obviously an angioma keratosum

Austregesilo: Arch. f. Schiffs-u. Tropen-Hyg. **16**: 622	1912	Negro	..	Both feet	Pernio	Resembled Madura foot	Atypical in all respects
Guszman: Orvosi hetil. **57**: 807.....	1913	.....	11	Left upper extremity	Pernio	Hemangiomatous	Lesion undoubtedly a nevus
Sibley: Proc. Roy. Soc. Med. **8**: 41.....	1914	Female	17	Backs of hands	"Chilblain circulation," cyanosed fingers; vesicles	None given	In discussion of this case, Dr. Adamson considered it hyperhidrosis with cheiropompholyx; lack of histologic data makes diagnosis of angiokeratoma doubtful
Fabry: Dermat. Ztschr. **22**: 16.....	1915	.....	11	Upper front part of thigh; also under left eye	No pernio; congenital	None given	Author made diagnosis of angioma of cheek and angiokeratoma circumscriptum of thigh, but the original lesion was congenital and this contraindicates a diagnosis of angiokeratoma
Paul: Brit. J. Dermat. **30**: 27.....	1918	.....	32	Face, forehead, chin, cheeks, nose, buccal mucosa and tongue; telangiectases of hard palate and conjunctival surface of eyelids	No pernio; nosebleed	Characteristic of angioma; no hyperkeratosis; no disease of blood vessels	Condition suggestive of congenital lesions, and pathologic study shows angioma
Weber: Brit. J. Dermat. **30**: 89.....	1918	Male	15	Lower extremity and gluteal region	No pernio	Atypical	Facts seem to indicate unilateral nevus rather than angiokeratoma, and the author made this suggestion in the title
Sibley: Proc. Roy. Soc. Med. **11**: 70....	1918	Male	21	Abdomen, scrotum, penis, dorsal and lumber regions; extremities; buccal mucosa	No pernio; pains in hands and feet	None given	Although discussion of physicians at the meeting of the Royal Society of Medicine tended to place this case as angiokeratoma, the atypical location, absence of pernio and absence of histologic study to confirm the diagnosis remove the case from this classification
Matsumato: Urol. & Cutan. Rev. **23**: 24	1919	Female	22	Margins of feet	Pernio	Angioma and hyperkeratosis	Lesion obviously an angioma
Fischkin: Arch. Dermat. & Syph. **3**: 104 (Jan.)	1921	.....	..	Lateral aspect of left thigh	No pernio	None given	Author stated that it was a congenital nevus vasculosus on which verrucous angiomatous lesions developed; history was obviously one of angioma
Sabouraud and Pignot: Bull. Soc. franç. de dermat. et syph. **30**: 355	1923	.....	14	Border of left hand; telangiectases of arms and legs	No pernio but numb fingers	None given	Visible tendency to generalized location, with no histologic study to confirm the diagnosis of angiokeratoma, removes this case from angiokeratoma
Richter: Dermat. Wchnschr. **80**: 574....	1925	.....	..	Tip of tongue	No pernio	Atypical; no disease of blood vessels	Atypical in every respect
Zeisler: Arch. Dermat. & Syph. **12**: 428 (Sept.)	1925	.....	..	Nose	No pernio	None given	Although clinical appearance was similar to angiokeratoma, no pathology was given to prove it; description suggests keratotic angioma or possibly lupus erythematosus
Van Rhee: Arch. Dermat. & Syph. **14**: 497 (Oct.)	1926	Male	36	Scrotum	No pernio	None given	Atypical in every respect, and no histologic study to confirm diagnosis
Stillians: Arch. Dermat. & Syph. **17**: 437 (March)	1928	Male	..	Scrotum	No pernio	None given	Wile considered these lesions similar to senile angiomas; patient showed no verrucous features, and no histologic study was given
Maki: Japan. Ztschr. f. Dermat. u. Urol. **12**: 8	1912	These men reported cases affecting the scrotum, but we regret that we were unable to obtain the details of their case reports, as the volumes in which the reports appeared were missing at the library of the Academy of Medicine					
Toyama: Japan. Ztschr. f. Dermat. u. Urol. **7**: 194 (Feb. 9)	1907						
Ito: Japan. Ztschr. f. Dermat. u. Urol. (June 6), p. 544	1908						

Following is the report of a case of angiokeratoma Mibelli, examined by us at the New York Skin and Cancer Hospital, and presented at a meeting of the New York Dermatological Society in February, 1930, by Dr. Traub, where the diagnosis was unanimously accepted.

REPORT OF CASE

History.—Miss S. F., aged 19 years, born in Poland, a stenographer, came to the clinic on Jan. 22, 1930, complaining of an eruption on the hands and feet. She stated that her mother had died of pulmonary tuberculosis. Her father, one brother and one sister were living and well. No other member of the family showed a similar or any other type of vascular disturbance of the skin. There was, however, an interesting history of nosebleed in the family, for the patient

Fig. 1.—View showing the distribution of the lesions on the dorsum of the hand and the fingers. The large mark on the little finger is an artefact.

said that she, as well as her sister and father, suffered from this condition. The patient suffered from frequent colds, but apparently had escaped practically all of the usual diseases of childhood. Three years previously she had had an attack of pneumonia, and one year previously, tonsillitis. For the past five and a half years she had had frequent nosebleeds; the condition sometimes became so severe that for weeks there was almost daily bleeding. For the past year and a half to two years, however, she had been practically free from this condition.

The patient stated that she had first noticed the eruption about six or six and a half years previously, shortly after her arrival in the United States. About ten or twelve years previously her hands and feet were frostbitten, and for two successive winters she had suffered from severe attacks of chilblains. This condition was treated by various types of bathing, as directed by her Polish physician. The first lesions appeared on the left index finger, and gradually others

Fig. 2.—General distribution of the lesions on the dorsa of the toes, particularly on the fourth and fifth toes.

Fig. 3.—Close-up view of the lesions on the index finger, giving an idea of the size and elevation.

developed, spreading to the other fingers of that hand. Two or three years later, she noticed that they had begun to develop on the right hand. Several of the toes on both feet had become involved in the past three years.

Clinical Examination.—Examination showed lesions ranging in size from that of a pinpoint to that of a pinhead on the fingers of both hands and the toes of both feet. The lesions were largely discrete, but in some areas they were so closely crowded together that they seemed to be confluent. The color ranged from a dull red to a dark purple, the central portion being almost black. On pressure,

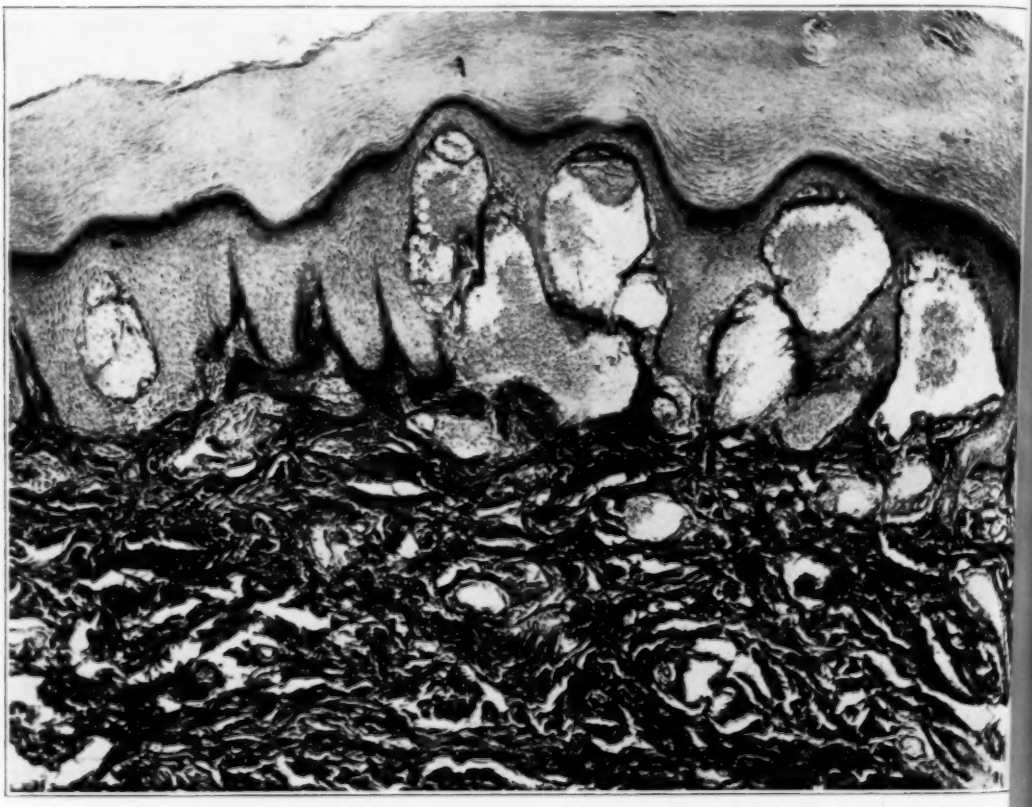

Fig. 4.—Note the marked hyperkeratosis and the presence of blood spaces and dilated blood vessels. Van Gieson stain; × 160.

the lesions did not entirely disappear, and the center was visible as a dark red puncta. Several of the larger and older lesions were elevated and had a distinctly warty appearance. There was a marked variation in the size of the lesions, apparently depending on their age.

Histologic Examination.—The section was made from a lesion excised from the index finger of the right hand. Low power examination showed that the epidermis was generally thickened throughout the diseased area. The corneal layer was prominent and considerably thickened. The rete pegs were lengthened and irregular in size and shape. Numerous small and large spaces were seen

throughout the upper half of the corium, especially in the papillary layer. Several apparently normal sweat glands were present, the ducts of which were compressed and in some places obliterated in the corneal layer. High power examination showed that the stratum corneum was quite thickened and that the cells of the upper part of the thickened corneum were not as flat as those of the lower part. This, however, may possibly have been due to faulty laboratory technic.

Fig. 5.—The elastic tissue fibers are broken up, and around the dilated blood vessels there is a definite loss of normal elastic tissue support. Weigert's stain; × 180.

The stratum lucidum and stratum granulosum were somewhat uniformly thickened but showed no unusual features. The rete malpighii was hypertrophied, and the basement membrane, although present, was poorly defined and in some places broken. The lacunae were large and irregularly oval, and some were filled with blood cells and coagulum.

In the examination of the section from our case no blood spaces were noted in the epidermis. The spaces were caused apparently by the disintegration of the papillary bodies. Close scrutiny revealed that their lining was made up of connective tissue cells and not of rete cells. We believe that these spaces were entirely in the corium, especially in the papillary layer, and although some appeared to be intra-epidermal, the picture was only an apparent one because the spaces, although apparently bounded by rete cells, showed intervening connective tissue cells that undoubtedly belonged to the papillary bodies.

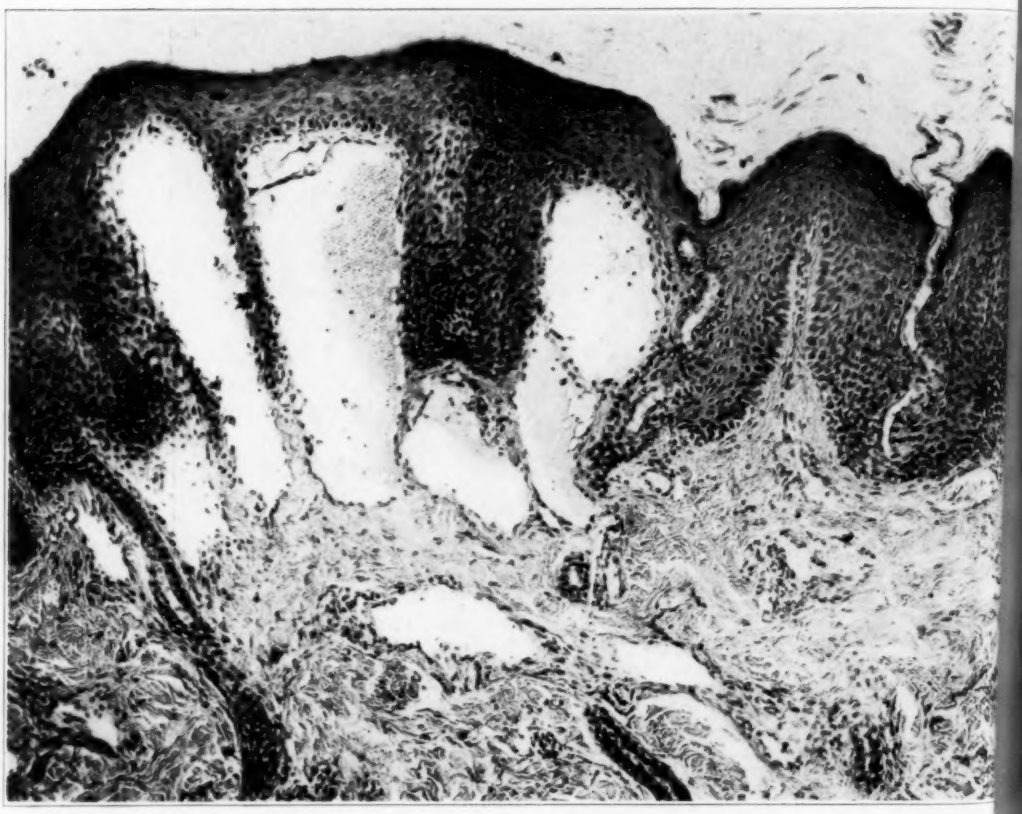

Fig. 6.—The blood "spaces" are lined by connective tissue cells. One of these spaces shows a definite septum traversing it. There is practically no cellular infiltration in the corium. Note the normal sweat ducts. Hematoxylin-eosin stain; × 160.

The upper part of the corium showed several large and small dilated blood spaces and vessels, a slight fibrosis in the region of the papillary bodies and, peculiarly, practically no inflammatory cellular infiltration. There were no unusual features in the lower part of the corium.

With Weigert's elastic tissue stain, it was apparent that there was a loss of elastic tissue support of the blood vessel spaces. Whether the weakness and breaking up of this elastic tissue support occurred first and were followed by a

dilatation, or whether the dilatation so stretched the elastin that a secondary breaking up of this tissue followed, has not been determined.

The formation of the blood spaces did not extend down into the corium as deeply as described by Mibelli in his case, and there was not the marked inflammatory infiltration that he pointed out.

COMMENT AND CONCLUSIONS

There was nothing in the histologic picture of our case (nor in the personal history of the patient) to bear out the contention of some authors that there is a relationship between tuberculosis and angiokeratoma. Brandweiner, Milian, Leredde, Pautrier, Jesionek,[14] Haury and Ehrman, among others, attempted to establish a relationship between the two conditions because of several instances in which patients who were afflicted with angiokeratoma also gave a history of tuberculosis. Ehrman went so far as to state that he observed tuberculous tendencies in three of four cases, and Tomasone expressed the belief that the lesions of angiokeratoma might be of a tuberculid nature. We agree with Jadassohn,[15] however, that there is not sufficient evidence to prove this.

In conclusion, we wish to reiterate that true cases of angiokeratoma, of which the case herein presented is an example, are rare, and that to fit into the classification they must incorporate the essential clinical, etiologic and histologic factors that Mibelli so ably described. Cases that are dissimilar in location and etiology, but that are identical histologically, must be included as true but atypical cases, and should be designated as angiokeratoma without pernio (Fordyce).

Cases resembling angiokeratoma clinically, but differing in etiology and histology, must be excluded from this diagnosis. For instance, angioma verrucosum and angiokeratoma Mibelli, although similar in clinical appearance, are etiologically and histologically not the same. Often senile angiomas become rough and warty in appearance and from the clinical picture may be mistaken for angiokeratoma. We repeat that angioma with keratosis is not angiokeratoma, for angiokeratoma does

14. Zeiler, Karl: Angiokeratoma (Mibelli), Prakt. Ergebn. a. d. Geb. d. Haut- u. Geschlechtskr., 1914, p. 421. Jadassohn, J.: Angiokeratom, in Mraček: Handbuch der Hautkrankheiten, Vienna, Alfred Hölder, 1907, vol. 4, p. 288. Besnier, E., in discussion of Brocq, M. L.: Un cas d'angiokeratome, Ann. de dermat. et syph. **3**:821, 1892. Unna, P. G.: Die Histopathologie der Hautkrankheiten, Berlin, August Hirschwald, 1894. Nobl, G.: Der varicose Symptomencomplex, Berlin, Urban & Schwarzenberg, 1910, p. 39. Dohi: Mitt. d. med. Gesellsch. zu Tokyo, 1900; cited by Matsumato: Urol. & Cutan. Rev. **23**:24, 1919. Bruckler: Ueber Angiokeratom, Kor.-Bl. d. mecklenb. Aerztever., Rostock, 1913, p. 841. Piffault: De l'angiokeratome, Thèse de Paris, July 26, 1893. Ogawa: Virchows Arch. f. path. Anat. **189**:433, 1907. Bettman: Dermat. Ztschr. **53**:38 (April 28) 1928.

15. Jadassohn (footnote 14, second reference).

not imply the existence of angiomatous tissue, but rather the presence of a disturbance in the blood vessels.

Hyperkeratotic tumors developing on congenital angiomas often present a clinical picture similar to Mibelli's description, but these must not be confused with angiokeratoma, for, unlike angiokeratoma, they develop from birth with the changes in the horny layer secondary to the congenital vascular changes.

It is difficult to say whether the fact that more cases have been reported in the foreign literature than in the American indicates that the condition is more common in Europe. Sutton, for instance, stated that he believed the condition was rare here and common in England. Since angiokeratoma is usually associated with pernio, it seems to us that the only definite way of determining such a fact would be to learn the frequency of the occurrence of pernio in Europe as compared with that in America.

In addition to the publications to which we have referred there are a number of dissertations on angiokeratoma without case reports.[14]

HISTOPATHOLOGY OF THE SKIN IN MYXEDEMA*

MAURICE J. REUTER, M.D.
MILWAUKEE

Because of the many conflicting reports and the uncertainty of knowledge concerning the exact pathologic changes in the skin in cases of myxedema, this study was undertaken. Special emphasis has been placed on the determination of the presence or absence of mucin or of a mucoid-like substance in the skin of patients with this disease.

Most of the sections of skin for study were taken from the left leg. Each section was divided into two parts. One part was fixed in alcohol and the other in formaldehyde; both were then blocked in paraffin, sectioned, mounted on slides and stained with the following stains: hematoxylin and eosin, van Gieson's, acid orcein counterstained with polychrome methylene blue, neutral orcein counterstained with polychrome methylene blue (for study of the collagen fibers), mucicarmine stain (Ochsenhirt [1]), Weigert's elastic tissue stain, elastin H and silver nitrate stain for melanin (Becker [2]). Kreibich's [3] method of staining for mucin was used also, but because it proved to be unsatisfactory it was discarded.

Twelve of the patients who formed the basis of this study had myxedema. One illustrative case will be reported.

REPORT OF CASE

A woman, aged 53, a housewife, came to the Mayo Clinic on June 27, 1929, complaining of weakness and dizziness of about two years' duration. She complained also of numbness and tingling of the hands and feet, a rough and scaly skin and a sallow color. Of late, she stated, she always felt cold, and she had noticed that she was not as alert mentally as in the past.

The skin was of a yellowish, waxy color, and edematous in appearance, and was covered with fine, dry scales. The basal metabolic rate was —34 per cent on two occasions. Examination of the blood revealed anemia. The remainder of

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1. Ochsenhirt, N. C.: The Significance of Mucus-Forming Cells in Carcinoma of the Large Intestine and Rectum, Surg. Gynec. Obst. **47**:32 (July) 1928.

2. Becker, S. W.: Melanin Pigmentation: A Systematic Study of the Pigment of the Human Skin and Upper Mucous Membranes, with Special Consideration of Pigmented Dendritic Cells, Arch. Dermat. & Syph. **16**:259 (Sept.) 1927.

3. Kreibich, C.: Muzinöse Bindegewebsdegeneration in der Haut (Färbung im Paraffinschnitt), Dermat. Wchnschr. **71**:539, 1920.

the general and laboratory examinations did not reveal abnormal features pertinent to this report. A diagnosis of myxedema was made.

On July 2, a small piece of skin was removed from the left leg for microscopic study. Evidence was found of moderate, uniform, relative and absolute hyperkeratosis, with distinct atrophy and almost complete flattening of the rete ridges. The epithelial cells varied considerably in staining; some of the nuclei took a heavy basic stain. In many of the cells of the rete there was also perinuclear vacuolization. In areas there appeared to be merging of the cytoplasm of the basal cells with the cutis; the cytoplasm stained faintly with eosin, and the nuclei lay at the upper poles of the cells. The corium was definitely thickened. In the upper layer of the corium there was homogenization of the collagen fibers, a tendency to take a basophilic stain with hematoxylin, sparse, perivascular infiltration with lymphocytes, and slight dilatation of the blood and lymph vessels. The upper and middle portions of the corium were edematous, and the collagen and elastic fibers were spread apart and fragmented. The connective tissue cells appeared to be slightly increased in number. Sections stained with the mucicarmine stain revealed the presence of material that stained red, which extended in a bandlike form throughout the upper part of the cutis, and which lay over and between the bundles of collagen. There was mucin-staining material in the deeper parts of the cutis. Under oil immersion, this substance appeared to be composed of fine threads and granules. This material was also especially prominent about the blood vessels and to some extent about the sweat glands. Evidence of collastin (a degenerative product of collagen) and of collacin (a degenerative combination product of collagen and elacin) was lacking, as it was impossible to demonstrate any tinctorial change with the acid orcein and neutral orcein stains.

A second biopsy was done on July 6. During the four days since the first biopsy the patient had been receiving desiccated thyroid extract. The microscopic features were essentially the same as those just described, except that the perivascular cellular infiltrate was more marked and the collagen fibers took a decided basophilic stain. With the orcein stains, changes were not noted in the collagen fibers.

This patient presented clinical and laboratory evidence of frank myxedema, probably of two years' duration. Under treatment with desiccated thyroid extract, improvement was rapid. When she was last seen at the clinic, Nov. 29, 1929, her general health was excellent except for occasional numbness and tingling of the fingers.

Besides the sections from the twelve cases of myxedema, sections of skin were obtained from ten cases in which the basal metabolic rates were below the normal average, but in which the classic subjective and objective signs of myxedema were lacking. These sections were obtained for study, principally to serve as controls for the cases with frank myxedema.

SUMMARY OF HISTOPATHOLOGIC CHANGES IN THE CASES OF MYXEDEMA

The epidermis gave evidence of moderate to fairly pronounced, uniform, relative and absolute hyperkeratosis, especially in the advanced cases of myxedema. Associated with the hyperkeratosis were hyperkeratotic plugs of the hair follicles and sweat ducts, and also keratotic plugs

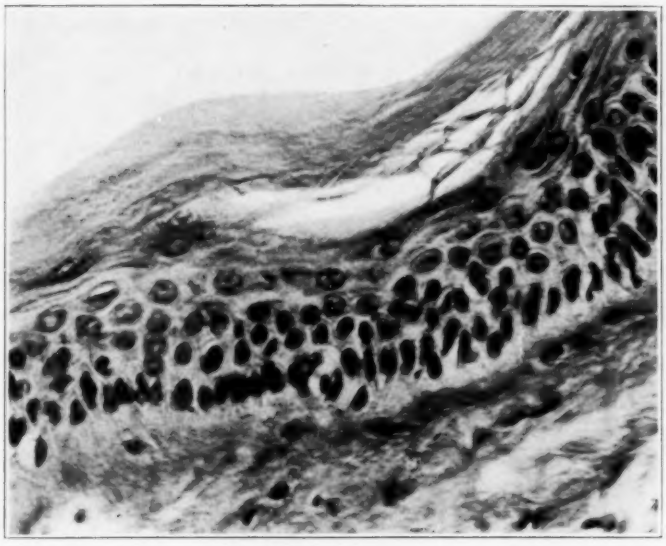

Fig. 1.—Hyperkeratosis, pyknotic changes in the rete and apparent merging of basal cells with the cutis. Van Gieson's stain; × 400.

Fig. 2.—Edema and dilated lymph vessels in the cutis with spreading apart of the collagen fibers. Hematoxylin and eosin; × 150.

not in relation to the hair follicles or sweat ducts. In the epidermis, also, there were varying degrees of atrophy of the rete; this was most marked in four of the cases of long standing. Irregularity in the reactions to staining in many of the epithelial cells, perinuclear vacuolization of many of the cells and disappearance of the interpapillary rete ridges were also noted.

In many of the sections, particularly in five cases, the cytoplasm of the basal cells stained faintly with eosin and seemed to merge with the cutis; the nuclei remained unaltered and confined to the upper poles of the cells. In the upper part of the cutis, in all the sections, there was

Fig. 3.—Marked hyperkeratosis with hyperkeratotic plugging in the epidermis. Inflammatory changes in the upper part of the cutis. Hematoxylin and eosin; × 90.

a mild degree of perivascular lymphocytic cellular infiltration associated with dilatation of the vessels and slight edema of the vascular walls. In eight of the cases, inflammatory changes were noted about some of the hair follicles, sweat ducts and sweat glands, together with atrophy of the follicles and sclerosis of the sweat glands. This was a pronounced feature of the microscopic picture in one case

In all of the cases there was homogenization of the collagenous tissue in the pars papillaris, and in some of the sections there was a

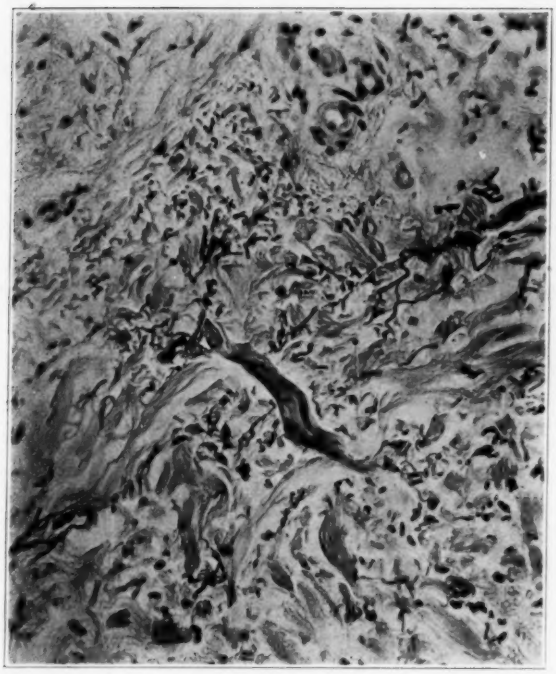

Fig. 4.—Edema of the cutis with splintering and fraying of the elastic tissue. Elastin H; × 250.

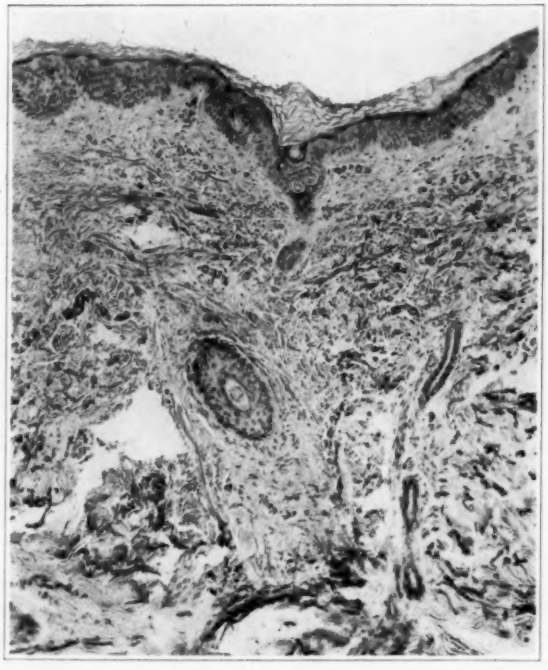

Fig. 5.—Hyperkeratotic plugging of the sweat duct, with inflammatory changes about the hair follicle and splintering of the elastic tissue. Elastin H; × 150.

tendency to stain with hematoxylin. The collagen and elastic fibers were spread apart, frayed and splintered in all of the cases; this was especially noticeable in nine advanced cases. In three cases, there was only moderate edema and spreading apart of the collagen and elastic fibers, together with splintering and fraying; these features were present only in portions of the upper part of the cutis, and were not at all prominent. The cutis was uniformly increased in thickness and was edematous; these changes were most marked in eight advanced cases. In one case there was edema only in the upper part of the cutis. In one case, there was an increase in the connective tissue of the corium and of the nerves.

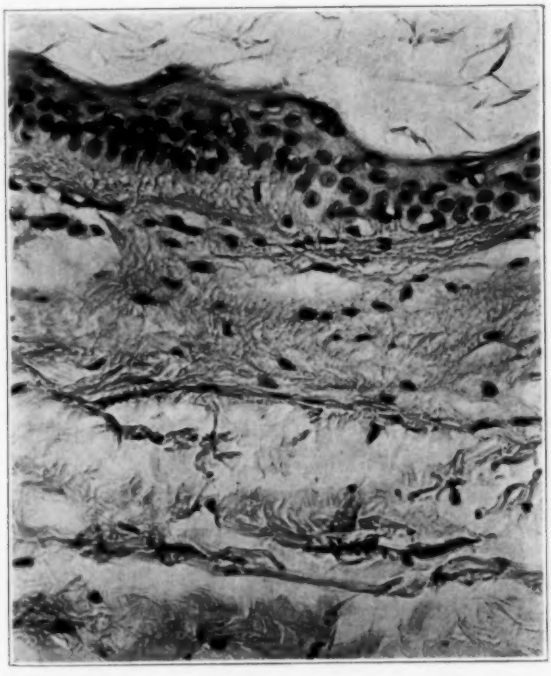

Fig. 6.—Edema and presence of mucin in the corium. Mucicarmine; × 300.

In all of the sections stained with the mucicarmine stain, bright, red-staining material was present. This was most marked in the upper part of the cutis, especially about the blood vessels, and to some extent about the hair follicles, but it was also irregularly distributed throughout the cutis and lay between and over the collagen fibers. In some cases, mucin was found in a narrow band lying just beneath the basal cell layer, and some of the basal cells contained mucin. In four cases in which treatment for myxedema had been given, there were only small amounts of mucinous material in the upper part of the cutis. Paradoxically, however, in the most advanced case of myxedema in our series, the least

amount of mucin was evidenced by the mucicarmine stain. The mucinous material, under oil immersion, appeared as fine granules and strands in all of the cases. In a few of the cases, the endothelial cells of the blood vessels and the cells of the sweat glands contained a small amount of this mucinous material.

The presence of melanin pigment in the skin was not at all a prominent feature of the microscopic picture, and in only three of the cases was there any appreciable increase in pigment. In these cases it was confined entirely to the basal cells.

SUMMARY OF HISTOPATHOLOGIC CHANGES IN THE CASES IN WHICH BASAL METABOLIC RATES WERE LOW BUT WHICH CLINICALLY WERE NOT CASES OF MYXEDEMA

For the most part, except for one case, the histologic changes corresponded in some respects to those of myxedema. The changes in the epidermis and corium were parallel, even to the presence of the substance in the corium that took the mucin stain. However, there was noticeable disagreement in the cases in respect to the edematous changes seen in the corium. In the cases of myxedema this was a pronounced feature, whereas in the cases in which metabolic rates were low it was, on the whole, of a negligible quantity. Again, the amount of mucin present in the cases with low basal metabolic rates was much less than that noted in the cases with myxedema.

DIFFERENTIAL DIAGNOSIS

From a histopathologic standpoint, the following must be considered in the differential diagnosis: scleroderma, chronic lymphangitis, elephantiasis, ichthyosis, general anasarca and localized edema of the extremities in association with exophthalmic goiter.

The histopathologic changes of scleroderma can be divided into two forms: the localized and the generalized. In the localized form changes of varying degree are seen in the epidermis, with a diffuse infiltrate of lymphocytes and plasma cells in the upper part of the cutis, destruction of the elastic tissue and homogenization of the connective tissue. In the diffuse form, the main process consists of hypertrophy of the preexisting collagenous bundles and periarteritis, periphlebitis, endarteritis and endophlebitis. Changes similar to those in the localized forms occur in the elastic and connective tissue. Later, the blood vessels are often occluded by the endarteritis, and atrophy of the epidermis and corium, together with atrophy of the adnexa, occurs. In both forms, increased melanin pigmentation of the basal cells may occur. Whereas mucin in the skin in this disease has been reported, its presence is not a constant occurrence.

The pathologic changes of recurrent lymphangitis are essentially those of recurrent erysipelas, as might be expected, since the process is the result of invasion of the superficial lymphatic structures by the streptococcus, and probably occasionally by the staphylococcus. Edematous changes are noted in the epidermis. The lymphatic channels are dilated, and there is stasis of lymph and an infiltrate of polymorphonuclear leukocytes, mainly perivascular in origin. Later, plasma cells accumulate and definite fibrosis sets in; this may lead to advanced changes of elephantiasis. The streptococci are found chiefly in the lymphatic channels.

In elephantiasis, microscopically, the fibrous tissue is greatly increased and extends deep into the cutis, and there is marked increase in the number of connective tissue cells. The arteries and veins are enlarged, their walls are thickened, the lymphatic vessels are enlarged and the lymph spaces are dilated. There also occurs perivascular infiltration of round, plasma and mast cells. Late in the process the sebaceous glands and hair follicles are atrophied. In the epidermis, hypertrophy is sometimes noted, whereas atrophy from pressure occurs in some instances. Hyperkeratosis is often noted. In summing up, the process can be said to be entirely inflammatory.

Ichthyosis, from the histopathologic standpoint, is characterized by marked hyperkeratosis, absence of stratum lucidum and small or absent stratum granulosum; the third of these characteristics is unusual in association with hypertrophy of the stratum corneum. The rete may be increased, or it is often decreased from an atrophied condition of the cells rather than from a decrease in their number. Both atrophy and increase in the rete may exist in the same patient in different regions. There is marked hyperkeratosis of the hair follicles, and often the epidermal portion of the sweat duct may be cornified. The sebaceous glands are usually atrophied. The lymph spaces, as a rule, are small. There may be an increase in mast cells in the corium, and also a perivascular cellular infiltrate. Edematous changes in the corium and accumulation of a mucinous substance in the corium are not recorded.

Extensive edematous infiltration of the skin and subcutaneous tissues is termed anasarca. The fluid is called a transudate, and is usually transparent and colorless, or yellowish, and may contain a variable number of erythrocytes and of leukocytes. The amount of fluid that may accumulate varies greatly. The epidermis is usually unaffected, although the cells may be edematous or atrophic. The fibers and cells of the connective tissue are usually pushed widely apart by the edema; the cells are likely to be more granular than normal and may contain droplets of fluid, or they may be atrophied.

The microscopic picture in localized solid edema of the extremities in association with exophthalmic goiter [4] is essentially one of an extreme degree of myxedema, so that differential diagnosis from the histopathologic standpoint may be impossible. All of the changes that were described as being characteristic of myxedema occur to a marked degree in this disease. The accumulation of mucinous substance which is found in large amounts just beneath the papillary layer, and which extends deeply into the corium and subcutaneous tissue, is especially characteristic of localized solid edema and is a much more pronounced histologic feature than it is in myxedema. Frequently there occurs a well demarcated border zone between the epidermis and the mucin. Edema of the pars papillaris and changes in the cells of the epidermis are not as prominent features as in myxedema.

COMMENT

In the main, the histopathologic changes in the various cases of myxedema which were studied consisted essentially of epidermal changes, associated with mild degenerative changes in the collagen and elastin, and the occurrence in the cutis of edema and a substance giving the histologic staining reaction of mucin. These changes have been described in part by a great number of authors. Gans'[5] description of the histopathology of the skin in myxedema tallies in most respects with mine. The changes in the epidermis are probably purely secondary, the result of interference with the nutrition of the epithelial cells by pressure from the edema and from the mucinous substance. The hyperkeratotic plugging of the hair follicles could be explained in some of the cases by the fact that the biopsy was obtained from the leg, where lesions of keratosis pilaris are present to some extent in practically all normal human beings. However, this would not explain the uniform hyperkeratosis. Beck,[6] who described in detail the changes in the epidermis, expressed the belief that they are pathognomonic for myxedema, especially the apparent merging of the cytoplasm of the basal cells with the cutis. Although this phenomenon was present in many cases, the changes were too widely scattered and occurred so irregularly that they could not be considered as pathognomonic. The perinuclear vacuolization of the epidermal cells, together with the irregularity in the staining of the cells, is a manifestation of edema and of interference with the nutrition of the cells.

4. O'Leary, P. A.: Localized Solid Edema of the Extremities in Association with Exophthalmic Goiter, Arch. Dermat. & Syph. **21**:57 (Jan.) 1930.

5. Gans, Oscar: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925-1928, pp. 127-130.

6. Beck, C., quoted by Gans (footnote 5).

Pigmentary alterations in the skin of myxedematous subjects, affecting chiefly the more exposed portions of the body, have been repeatedly emphasized, most recently by Krantz and Means.[7] Histologically, increase in pigmentation was seen in only three cases. In these cases, the pigment was confined to the basal cells and was definitely melanin, as was brought out by the silver nitrate stain. However, the fact that the sections of skin were taken, for the most part, from the unexposed parts of the body, could explain the absence of increased pigmentation in most of our sections. Clinically, an increase in pigmentation was not noted.

The hyperkeratosis and the hyperkeratotic plugging of the hair follicles and sweat ducts, along with the inflammatory fibrotic and atrophic changes that were noted about many of the hair follicles and about occasional sweat glands, fits in well with the cutaneous manifestations of the disease; namely, the fine, dry, scaling of the skin, the typical lesions of keratosis pilaris, the diminished sweating and the gradual loss of hair.

The dilated blood vessels, and the perivascular lymphocytic cellular infiltrate in the upper part of the cutis, suggest that it is merely an irritative reaction in this region from the presence of the mucinous collections in the cutis. Again, these changes are a common accompaniment of ordinary edema in the skin. There were no changes in the vessels other than slight edema of the vascular walls in a few cases. Obliterating endarteritis, as has been described, was not present in any of our cases. In the sections studied, marked degenerative changes in the collagen, including tinctorial changes in staining reaction when Unna's special collagen stains were used, as reported by many observers and especially by Unna,[8] were not observed. However, there was evidence of homogenization of the collagen in the upper part of the cutis and a tendency to stain with hematoxylin. The collagen fibers in the deeper layers of the cutis were fairly normal, except for the fact that they were widely separated, frayed and splintered by the edema, and by the accumulation of the mucin throughout the corium. Confirmation was also lacking as to the observation of Virchow[9] and others that the connective tissues were rich in cells and nuclei, as the connective tissue cells for the most part were not numerous and were present in numbers only in the normal skin.

There was a definite relationship between the degree of myxedema clinically and the histopathologic changes in the skin, particularly the

7. Krantz, C. I., and Means, J. H.: Pigmentation in Myxedema, Boston M. & S. J. **195**:518 (Sept. 9) 1926.

8. Unna, P. G.: The Histopathology of the Diseases of the Skin, New York, The Macmillan Company, 1896, pp. 991-997.

9. Virchow, R.: Ueber Myxoedema, Berl. klin. Wchnschr. **24**:121 (Feb.) 1887.

changes in the epidermis and the edematous appearance of the corium. However, this same relationship did not hold true in regard to the mucin. Paradoxically, in the most advanced case of myxedema in the series, but little mucin was made evident with the mucin stain; however, this may have been the result of inadequate staining. This variability of the mucin content in many of the cases leads to the assumption that the clinical appearance of the skin in myxedema is chiefly the result of the edema. In all probability, in the fixation of the tissues a great deal of the edematous fluid is lost. This might have been overcome to some extent by the fixation of the tissues in boiling formaldehyde, and in this way the edematous fluid might have been better preserved.

It is most difficult to offer a satisfactory explanation for the changes in the skin seen in the cases in which there were low basal metabolic rates but in which clinical signs of myxedema were absent. As previously mentioned, the histologic changes in the skin in these cases corresponded in some respects with those seen in myxedema, except for the fact that the edematous changes were much less pronounced. The presence of the substance which stained with mucin is apparently normal, as may be noted later. In view of the lack of knowledge concerning patients with low basal metabolic rates but no clinical signs of myxedema, I feel that further comment on the significance of this substance at this time would be futile.

At the beginning of this study it was felt that knowledge of the histopathologic features of the skin in myxedematous subjects might be of decided help in diagnosis, especially in distinguishing cases of myxedema from cases in which metabolic rates were low but clinical signs of myxedema were absent. However, the similarity of the histologic picture seen in these two types of cases definitely excludes histopathologic study of the skin as a diagnostic aid, with our present tinctorial methods of study. Of interest in this connection are the observations of Lueg and Grassheim [10] who stated that in exophthalmic goiter and myxedema the basal metabolism and the capacity of the skin for polarization are parallel. They stated that in the diagnosis of diseases of the thyroid gland, the determination of the capacity of the skin for polarization is as important as the determination of the basal metabolism.

MUCIN

The structure of mucin and allied substances has remained in obscurity until recent years. The information given in textbooks in regard to mucin is in general limited to that of its solubilities and some

10. Lueg, Werner, and Grassheim, Kurt: Welche Folgerungen lassen sich für die Schilddrüsenfunktion durch vergleichende Untersuchungen von Grundumsatz und Polarisationskapazität der menschlichen Haut ziehen? Ztschr. f. klin. Med. **110**:531, 1929.

other of its physical properties. According to Hawk, mucin belongs in the group of conjugated proteins called glycoproteins, compounds of the protein molecule with a substance or substances which contain a carbohydrate group other than nucleic acid. Exact knowledge is lacking concerning the mode of union between the sugar and the rest of the molecule. Mucins was the term given by Hawk to those forms of glycoproteins which occur in the secretions and fluids of the body. He stated that mucoid material is present in connective tissue, elastic cartilage and osseous tissue.

Mallory and Wright [11] stated that the term mucin is applied to a proteid substance which has certain chemical reactions and to certain other substances which give the same reactions but do not belong to the group of proteids. These various substances of secretory and degenerative origin cannot be distinguished microscopically and have been investigated but little chemically. Mathews [12] found small amounts of mucoid material in the corium of the steer, cow and goat. Schafer [13] stated that mucus is present in the body not only as a product of epithelial cells and mucous glands, but also in the form referred to as mucoid tissue, as found in cartilage, bone, blood serum, the aorta, the vitreous humor of the eye and in the umbilical cord. He said that it is almost universally distributed in the body as the cementing substance in the interstices of connective tissue cells, endothelial cells and epithelial cells, in which case it is called tissue mucin. Chemically, according to Lewis and Stöhr,[14] there are many varieties of mucin; true forms of mucin are formed in abundance in goblet cells and mucous tissue, and to a less extent they occur in all embryonic connective tissue. Related substances, called mucoid, are found in tendon, cartilage and bone. In the umbilical cord, mucin may be regarded as a secretion which is produced and discharged from all the surfaces of the cells.

Delafield and Prudden [15] stated that mucous degeneration may occur in the cells or in the intercellular substance under many conditions, such as abnormal increase in the functions of the cells and sometimes as an entirely abnormal transformation of the cells. In certain cases, as in tumors, the intercellular substance may undergo conversion into mucin-containing material and may lose its original structure.

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11. Mallory, F. B., and Wright, J. H.: Pathological Technique, ed. 8, Philadelphia, W. B. Saunders Company, 1924, pp. 191-193.

12. Mathews, A. P.: Physiological Chemistry, ed. 4, New York, William Wood & Company, 1925, pp. 323-326.

13. Schafer, E. A. S.: The Essentials of Histology, ed. 11, Philadelphia, Lea & Febiger, 1920, p. 94.

14. Lewis, F. T., and Stöhr, Philipp: A Text-Book of Histology, Philadelphia, P. Blakiston's Son & Company, 1913, p. 62.

15. Delafield, Francis, and Prudden, T. M.: A Text-Book of Pathology, ed. 13, New York, William Wood & Company, 1915, pp. 54-56.

In a search through the literature, definite statements could not be found regarding the presence of mucin in the normal human skin, other than the fact that mucin occurs in the interstices of the connective tissue. As a means of control of the cases with myxedema and low basal metabolic rates, a number of sections of normal skin were stained with mucicarmine. In all the sections studied, mucinous-staining material was present in very small amounts, and although the amounts were much smaller than in the myxedematous skin, it was so constantly present that it probably can be regarded as a normal constituent of the skin.

From the foregoing comment it can be seen that mucin is widely distributed throughout the body, that it is a normal part of the interstices of connective tissue, and that, in my experience, it is disclosed by tinctorial methods in very small amounts, on careful search, in the normal skin. Information as to its exact chemical nature is being awaited from the biochemist. Finally it must be remembered that the term mucin does not refer to a single chemical entity.

Staining of Mucin.—According to Carleton,[16] from the histochemical standpoint mucin has the following characteristics: great affinity for basic dyes in general, due to the acid reaction of mucin; metachromatic staining with certain basic aniline dyes; solubility in weak alkalis, and precipitation by acetic acid.

Most authors state that mucin is coagulated into threads by alcohol and corrosive mercuric chloride, and that in this form it can be stained by a number of staining reagents. Various aniline dyes are used for staining mucin, such as polychrome methylene blue and thionine. Kreibich,[17] and more recently Lillie,[18] reported new methods for the staining of mucin. The mucicarmine stain of Mayer, as used in this study, is generally considered as specific for mucin. The impression was gained in this study that the mucicarmine stain displayed a tendency to become diffused, giving a false reaction with some of the collagen fibers.

As to the origin of the excess of mucin in the myxedematous skin, definite conclusive evidence was lacking. The possibilities in regard to the mucin are that it is the result of degenerative changes in the collagen, that it is the direct product of the connective tissue cells, or that it is the result of a mucinous infiltration into the skin, caused by the disturbed function of the thyroid gland. The majority of the early observers

16. Carleton, H. V. M.: Histological Technique for Normal Tissues, Morbid Changes and the Identification of Parasites, New York, Oxford University Press, 1925, p. 176.

17. Kreibich, C.: Mucin bie Hauterkrankung, Arch. f. Dermat. u. Syph. **150:** 243 (May) 1926; **153:**799 (Oct.) 1927.

18. Lillie, R. D.: Brief Method for Demonstration of Mucin, J. Tech. Methods **12:**120 (March) 1929.

believed that the increase in mucin in the skin was the result of the reversion of the connective tissue to that of an embryonal type, and that the ground substance of this embryonal type of tissue was rich in mucin. Recently, Kreibich, who has studied extensively the occurrence of mucin in cutaneous disease, championed a similar theory; namely, that mucin is a trophic product of abnormally placed fibroblasts, that it is found around young, immature fibroblasts, and that it diminishes in quantity in old connective tissue. By histochemical means, in a great many cutaneous diseases, he found mucin to be present in the skin wherever there was proliferation of new connective tissue.

If this hypothesis as to the origin of mucin is accepted, it would be expected that, in the myxedematous skin, evidence would be found of primitive connective tissue, in which the fibroblasts are greatly increased in number. Increase in connective tissue and in the number of fibroblasts, as has been described previously, was not noted; so it does not seem reasonable that this process can account for the presence of the excess of the mucinous-staining substance in myxedema. The corium was definitely increased in thickness in the advanced cases of myxedema, and in some of the sections there was swelling of the collagen fibers. This increased depth of the cutis is apparently due to the presence of edema and of the mucinous-staining substance in the corium, which spread apart and fray the collagen and elastic fibers and add to the bulk of the skin as a whole. In this way the clinical characteristics of the disease are produced. As a result of personal observation, I am in accord with Gans who stated that the mucin-like bodies are seemingly situated between the connective tissue fibers rather than being produced by degeneration of the fibers themselves. The collection of the mucinous-staining material, especially about the blood vessels and hair follicles, as we have noted, suggests decidedly that it is the result of infiltration into the skin by way of the blood vessels.

SIGNIFICANCE OF EDEMA AND MUCIN

Magnus-Levy,[19] in 1904, showed that there is an accumulation of albumin in cases of myxedema and it was assumed that the affinity of this albumin for water explained the peculiar edematous appearance of the skin. He further stated [20] that American authors take the view that the altered consistency of the subcutaneous tissue is merely due to the fact that ordinary edema fluid is deposited in a different manner in cases

19. Magnus-Levy, A.: Ueber Myxödem, Ztschr. f. klin. Med. **52**:201, 1904.

20. Magnus-Levy, A.: Metabolism in Diseases of the Ductless Glands, in Von Noorden, C.: Metabolism and Practical Medicine, Chicago, W. T. Keener & Company, 1907, vol. 3, p. 983.

of myxedema than in cases of edema proper; that is, in myxedema the edema lies in the tense and deeper parts of the connective tissue.

Foster [21] stated that it had been recognized for some time that the secretion of the thyroid gland has a definite influence on the water metabolism of the body and that, since Tatum [22] had demonstrated hydropic changes in the cells of organs of thyroidectomized rabbits, it was possible that the disturbance of metabolism in myxedema was due primarily to changes in permeability of cellular membranes. Foster stated, also, that the experiments of Embden,[23] which indicate that thyroid extract when added to certain solutions increases the rapidity with which the solution passes in vitro through a membrane, are of significance in these considerations.

Boothby [24] and others have shown that the edema of myxedema and of cardiac edema are unlike, in that the nitrogen content of the former is higher than that of blood serum, whereas the nitrogen content of edema of cardiac origin is very low. These investigators have shown that there is a definite relation in myxedema between the total loss of water and the total loss of nitrogen in subjects who have been given thyroxin and desiccated thyroid material. In three cases the nitrogen was approximately 1.9 per cent of the water. They suggested that the edema of myxedema is due to an albuminous colloid fluid, with a nitrogen-water ratio higher than the accepted average of 1.1 per cent for human serum and identical with that of egg white. Nitrogen composes 2 per cent of egg white, definitely less than that of muscle, which contains more than 3 per cent of nitrogen. These results support the hypothesis that in myxedema there is retention in the body of an excessive amount of albuminous fluid or of "deposit protein" which is associated with water and is responsible for the characteristic "solid edema." Boothby and his collaborators also showed that in patients with myxedema there was a definite increase in concentration of blood urea when the patients were given desiccated thyroid extract. This indicates retention through renal impairment, possibly due in part to the mechanical effect of edema of the kidney. The increase in blood urea occurred at the time when greatest elimination of nitrogen occurred in the urine. These facts show that the edema fluid mobilized by the thyroxin contains large quantities of nitrogen, and they confirm the fact that the edema of myxedema

21. Foster, N. B.: Myxedema, in Nelson's Loose-Leaf Medicine, New York, Thomas Nelson & Sons, 1928, vol. 3, p. 292.

22. Tatum, A. L.: Morphological Studies in Experimental Cretinism, J. Exper. Med. **17**:636, 1913.

23. Embden, quoted by Foster (footnote 21).

24. Boothby, W. M.; Sandiford, Irene; Sandiford, Kathleen, and Slosse, J.: The Effect of Thyroxin on the Respiratory and Nitrogenous Metabolism of Normal and Myxedematous Subjects, Tr. A. Am. Physicians **15**:195, 1925.

is probably due to an albuminous fluid. Thompson [25] and his collaborators found a high protein content in the cerebrospinal fluid in most cases of myxedema, which dropped to a normal level when preparations of thyroid gland were given. They conjectured that this phenomenon is possibly related to the storage of nitrogenous substances in general in cases of myxedema.

This study tends to confirm the work of Boothby and others. The finding of edema and the presence of mucinous-staining material, which, according to present histologic methods must be regarded as mucin, bears out their belief that the retention of an albuminous or protein fluid is the cause of the edema of myxedema. Horsley [26] and Halliburton [27] were able to show an increase in mucin in the skin, tendons, salivary glands and blood of animals from which the thyroid glands had been extirpated and Schlagenhaufer and Wagner [28] were able, in sporadic cretinism, to show changes in the skin similar to those in myxedema. Further, Levin,[29] in 1900, as a result of his experiments on dogs, supported the contention of Horsley that myxedema is due to autointoxication with mucin. I feel, in part, that there must be a return to the original contention of Horsley, that in myxedema there is a specific accumulation of mucinous or albuminous material in the skin, and in all probability, in all the structures of the body. This might account for many features of the disease.

The term mucin has been used rather freely throughout this paper. Justification for its use lies only in the fact that the material present in the myxedematous skin stained as mucin with the so-called mucin stains. At present those substances which stain with mucicarmine should be designated as mucin, until some other histochemical method of differentiation is developed. At the present time, such means of differentiation are inadequate.

SUMMARY

The significant histologic changes in myxedema are as follows: Fairly uniform hyperkeratosis of the epidermis, with hyperkeratotic plugging of the hair follicles and sweat ducts; irregular, scattered atrophy of the epidermis, with degenerative changes in the epidermal cells; pro-

25. Thompson, W. O.; Thompson, P. K.; Silveus, Esther, and Dailey, Mary Elizabeth: The Protein Content of Cerebrospinal Fluid in Myxedema, J. Clin. Investigation **6**:251 (Oct.) 1928.

26. Horsley, Victor: The Thyroid Gland: Its Relation to the Pathology of Myxoedema and Cretinism, Brit. M. J. **1**:211 (Jan. 31) 1885.

27. Halliburton, W. D.: Mucin in Myxoedema—Further Analyses, J. Path. & Bact. **1**:90, 1893.

28. Schlagenhaufer and Wagner, quoted by Gans (footnote 5).

29. Levin, Isaac: Physiological Studies in Mucine, Am. J. Physiol. **4**:90 (July) 1900.

nounced edematous changes in the corium, and in consequence a spreading apart of the collagen and elastic fibers associated with mild degenerative changes; a sparse cellular infiltrate about the vessels in the upper part of the cutis, and in a few cases about the hair follicles and sweat glands; and the constant presence of a mucinous staining material in considerable quantities. The characteristic clinical appearance of patients with myxedema is, in all probability, the result of edema and the presence of the excess of mucin in the corium. In cases in which the basal metabolic rates are low but in which myxedema is not present, the cutaneous histologic picture is similar to that seen in myxedema, except for the absence of marked edematous changes. The histopathologic picture in the skin of myxedematous patients is not diagnostic. Mucin is probably a normal constituent of the skin. Knowledge concerning mucin is meager, and at present reliance must be placed on tinctorial histologic methods for its detection.

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA (HABERMANN)

REPORT OF A CASE *

F. A. DIASIO, M.D.
Assistant Visiting Dermatologist, Lincoln Hospital
NEW YORK

Within the last fifteen years, an apparently unusual condition characterized by papular lesions that show a tendency to crusting, necrosis, hemorrhage and, following the disappearance of the necrotic papules, varioliform scarring and pigmentation, has been described in the European and British literature under the title of "pityriasis lichenoides et varioliformis acuta."

The disease was named by Habermann,[1] although it had been described originally by Mucha[2] in 1916. According to Wise and Sulzberger,[3] who have recently added their case to the literature, about forty examples of this condition have been reported. A complete bibliography up to 1928 is given by F. Juliusberg,[4] and a more recent survey of this disorder may be found in a report by Senear and Oliver.[5]

The condition affects males predominantly. The lesions show a remarkably uniform distribution, the trunk, mainly on its anterior aspect and the extremities, especially the flexor surfaces, being involved. The exanthem is polymorphous and symmetrical. The disease begins with a reddish macule with central vesiculation. Later it becomes a firm, smooth, waxy, pinkish or reddish brown papule, round or oval, varying in size from that of a pinhead to that of a pea, and having, at times, a scaly collaret. Usually the "lichenoid" papule develops a

* Submitted for publication, Oct. 28, 1930.

* Read (in abstract form) before the Lincoln Hospital Alumni Association, Monday, Oct. 20, 1930.

1. Habermann: Dermat. Ztschr. **45**:42, 1926.

2. Mucha: Arch. f. Dermat. u. Syph. **123**:586, 1916.

3. Wise, F., and Sulzberger, M. B.: Pityriasis Lichenoides et Varioliformis Acuta (Habermann), M. J. & Rec. **132**:331 (Oct. 1) 1930.

4. Juliusberg, F.: Die Erythrodermien, in Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7 (teil 1), p. 311.

5. Senear, F. E., and Oliver, E. A.: Pityriasis Lichenoides et Verioliformis Acuta (Habermann), Arch. Dermat. & Syph. **23**:12 (Jan.) 1931.

distinct central vesiculation which is soon superseded by necrosis and the appearance of a hemorrhagic crust at the summit. When the crust eventually falls off, a depressed scar marks the site of the former lesions. Occasionally, pigmented areas are all that are left behind, scattered indiscriminately among the active elements.

The eruptive manifestations show a tendency to appear in crops. The duration of each outbreak of new lesions is short, while the disease itself may last from three weeks to two years. In spite of the fact that this clinical entity is a self-limiting disorder, I am convinced, from a study of the literature as well as from my personal experience with my case, that there are subacute and chronic types of pityriasis lichenoides et varioliformis, and that therefore the use of the suffix "acuta" suggested by Habermann in many instances is untenable. Wise [6] takes a similar stand.

No etiologic factors of pityriasis lichenoides et varioliformis acuta (Habermann) have been determined, so that the exact nosologic position of this disease remains obscure. However, previous to Mucha's description and Habermann's naming of this clinical entity, pityriasis lichenoides et varioliformis acuta, on account of its close resemblance to the clinical picture of pityriasis lichenoides chronica, any example of parapsoriasis, irrespective of its clinical type, on microscopic examination was said to present the same histologic changes, namely: a low grade, exudative, inflammatory process associated with a disorganization of the basal cell layer, hydrops of some of the epidermic cells in the prickle cell layer and, at times, even parakeratosis. Satenstein,[7] in his vast dermatopathologic experience, has never observed necrosis or vesicles and bullae in parapsoriasis, which never leaves atrophy as a sequel. Since the recognition of the so-called varioliform type of parapsoriasis, e. g., pityriasis lichenoides et varioliformis acuta (Habermann), parapsoriasis varioliformis (Wise),[8] necrosis and the development of vesicles and bullae have been observed often enough on microscopic examination of these cases to warrant the opinion that pityriasis lichenoides et varioliformis acuta may be a distinct and separate entity having no nosologic relationship to the parapsoriases. Instead of considering this dermatosis "a rare subvariety of parapsoriasis" as Wise does, Satenstein believes that "we are dealing most likely with a new disease with an old name."

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6. Wise, F.: Personal communication.

7. Satenstein, D. L.: Personal communication.

8. Wise, F.: Parapsoriasis: Suggestions for simplifying its nomenclature and classifying its clinical varieties for teaching purposes, New York State J. Med. **28**:901 (Aug. 1) 1928.

REPORT OF CASE

History.—J. L. M., aged 40, a first mate on one of the coastal steamers, married, was referred to me by Dr. R. E. Castelli on Sept. 3, 1930. The patient complained of an obstinate and recurring eruption, limited to the covered parts of the body, and of two years' duration. Although the "rash" was not accompanied

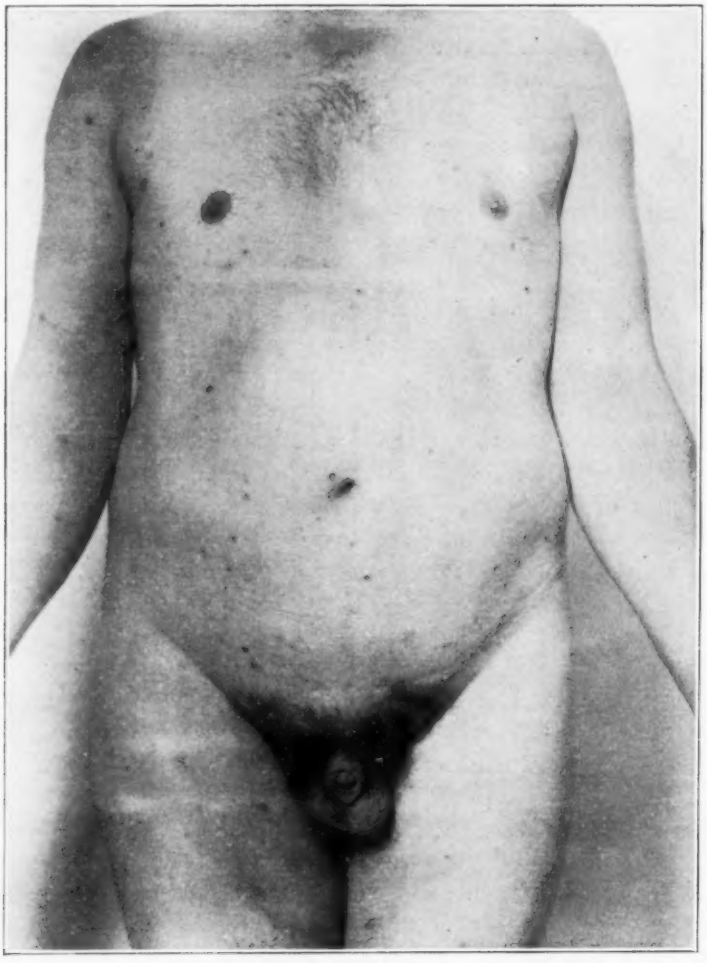

Fig. 1.—Note the bilateral, symmetrical and polymorphous features of the eruption.

by any subjective symptoms, he objected, for cosmetic reason, to its existence, and was thus very anxious to get rid of it.

There was no history of tuberculosis or other chronic disease in the family. He had been married eleven years and had never had extramarital exposures. A balanoposthitis about eighteen months ago was the only genital lesion he had ever had. His children were living and well. There was no history of malaise, sore

throat or other general symptoms. He had enjoyed good health and had worked hard in the past. For the past year or so, he had been constipated, and for relief had taken "salts" at least once a week. Recently a few teeth had been extracted.

Two years before examination, he first noticed on the abdomen a few reddish spots. Gradually similar spots appeared on the rest of the trunk and on the

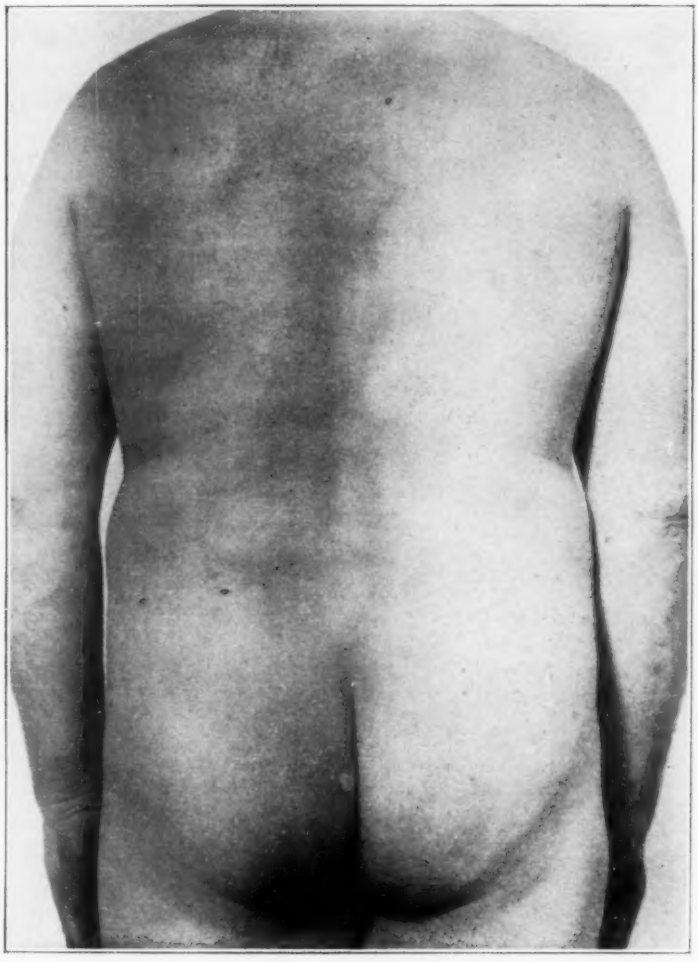

Fig. 2.—Showing the relative diminution of the eruptive manifestations on the back and the extensor surfaces when compared with Fig. 1.

thighs. Later, the arms and back were involved. The anterior part of the trunk and the flexor aspects of the extremities were favored. About the armpits, also, the spots seemed to be more abundant. As the spots became larger and elevated above the normal skin, they crusted over. When the "bloody" crust fell, he always noted a scar and at times a brownish discoloration in its place. New spots appeared in crops to replace those of a previous crop which had involuted and

disappeared. The eruption had thus persisted at varying intervals for the past two years. Most of the physicians who examined the patient made a diagnosis of syphilis and treated the patient for that disease, until he became discouraged and sought relief elsewhere.

Physical Examination.—The patient was well developed, robust and plethoric. The face, neck, hands and forearms were tanned dark brown. The scalp, ears,

Fig. 3.—Note the absence of grouping, the polymorphism and the dissemination of the lesions. A few varioliform scars are seen on the thigh.

nose and throat showed no pathologic condition. The pupils were equal and reacted to light and in accommodation. The chest was barrel-shaped; the lungs were clear, and the heart did not show any arrhythmia or any change in the heart sounds. The abdomen was protuberant and no notable abnormalities were present except tympanites. Some tenderness was elicited below the xiphoid process.

There were no deformities or other visible alterations of the extremities except a deep, oblique scar on the dorsum of the left hand, close to the base of the thumb. The reflexes were not increased or absent. The lymphatic glands were not noticeably enlarged. The mucous membranes were clear, as was the anal region. The blood pressure was 125 systolic and 90 diastolic.

On the covered portions of the body (trunk, thighs, arms and shaft of the penis), there was a bilateral, symmetrical, disseminated and polymorphous eruption consisting of macules, maculovesicles, maculopapules, necrotic and crusted papules,

Fig. 4.—Low power magnification of a maculovesicle. Note the development of the vesicle, the presence of red blood cells within the cavity and the moderate interstitial edema of the cutis.

small ulcers, varioliform scars and pigmented spots, all intermingled and scattered in varying profusion on different areas of the skin (figs. 1, 2 and 3). The papular lesions were predominant, while the maculovesicles were the fewest and were inconspicuous. The larger and older hemorrhagic and crusted formations stood out well in this intermingling of different types of lesions. The reddish macules with the deep-seated vesicles were the earliest manifestations of the disease and were superseded by firm reddish or brownish papules, varying in size from that of a

pinhead to that of a pea. These papules were round or oval, and had flat or cupoliform tops. Some presented a deep, central vesiculation; others appeared waxy and glistening, with smooth tops; the remainder were scaly and dull or displayed at the periphery a scaly collaret. Some of the papules later became necrotic and were capped by hemorrhagic crusts which were fairly adherent and represented late lesions. When a crust was forcibly removed, a deep, granular ulcer was noted, which bled slightly. Likewise, when the scaly papules were scratched, no bleeding points were seen.

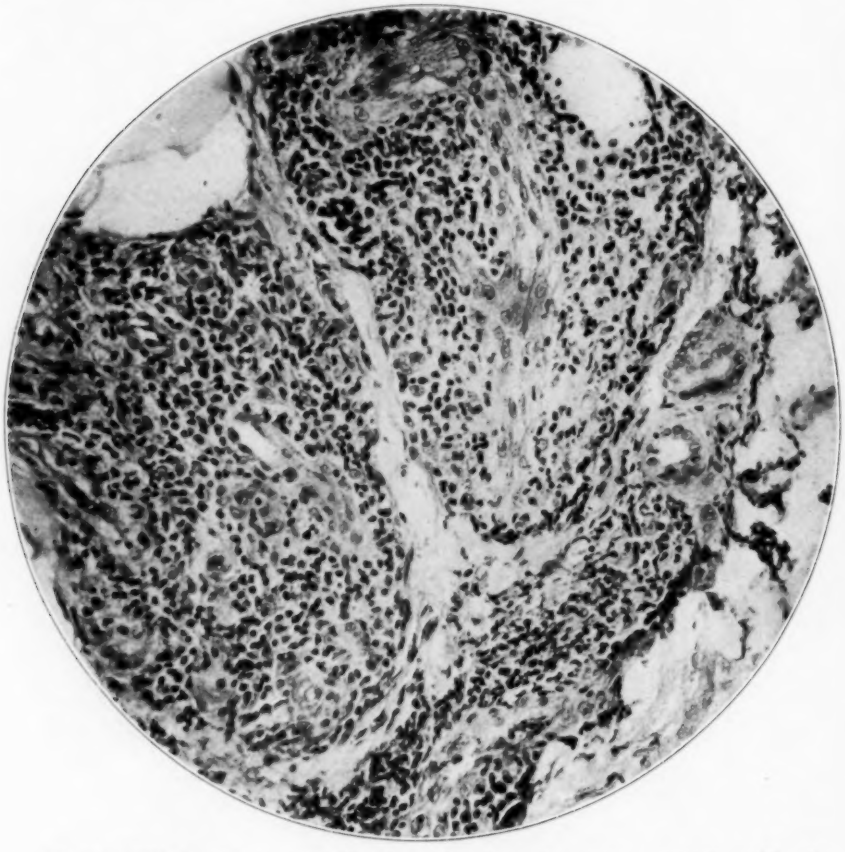

Fig. 5.—High power magnification showing the acute necrosis with the broken-down cells clumped up in the form of granules.

The eruption did not follow the lines of cleavage of the skin. The various types of lesions were scattered over the affected areas without any tendency toward grouping, in spite of the fact that the eruption was sparse on the back of the trunk and on the extensor surfaces of the extremities. On the shaft of the penis there were four lesions in various stages of development.

In addition to the lesions exhibiting stages of development ranging from the reddish macule to the necrotic and crusted papules, there were about a dozen depressed scars and a few brownish areas at the site of lesions of former outbreaks.

Laboratory Examination.—Three consecutive Wassermann tests were negative. The routine urinalysis showed no abnormality. The chemical analysis of the blood did not reveal any pathologic deviation from normal. The blood picture failed to show any morphologic alterations or the presence of abnormal constituents in the blood. The blood count was essentially negative. The hemoglobin was slightly reduced (85 per cent).

Microscopic Examination.—Three lesions (a maculovesicle, a "lichenoid" papule and a crusted papule) were removed under local anesthesia. They were fixed, stained and prepared in the usual manner. D. L. Satenstein reported as follows:

Fig. 6.—Low power magnification of a lichenoid papule. Note the absence of a dividing line between the epidermis and the cutis. Note also the interstitial edema and parakeratosis.

Maculovesicle: There were two distinct processes present (figs. 4 and 5). Under the epidermis (in the subepidermic zone) there was what appeared to be a sudden development of vesicles, evidenced by the fact that the papillary bodies in the upper cutis formed the base of the vesicle, while the roof was covered by the entire epidermis. Within this cavity (i. e., the vesicle) there were blood cells. The entire cutis showed a moderate interstitial edema. In the deep cutis and

subcutis (in the region of the coil glands) and within the fat, there was a fairly marked cellular infiltration about the vessels.

Under the high power lens, there was noted in the central mass a conglomeration of lymphocytes, polymorphonuclear leukocytes, broken-down cells clumped up in the form of granules and some granular degeneration of the connective tissue. The picture was that of an acute necrosis (almost), and it was found near the coil glands. In the fat proper, away from the coil glands, there were lympho-

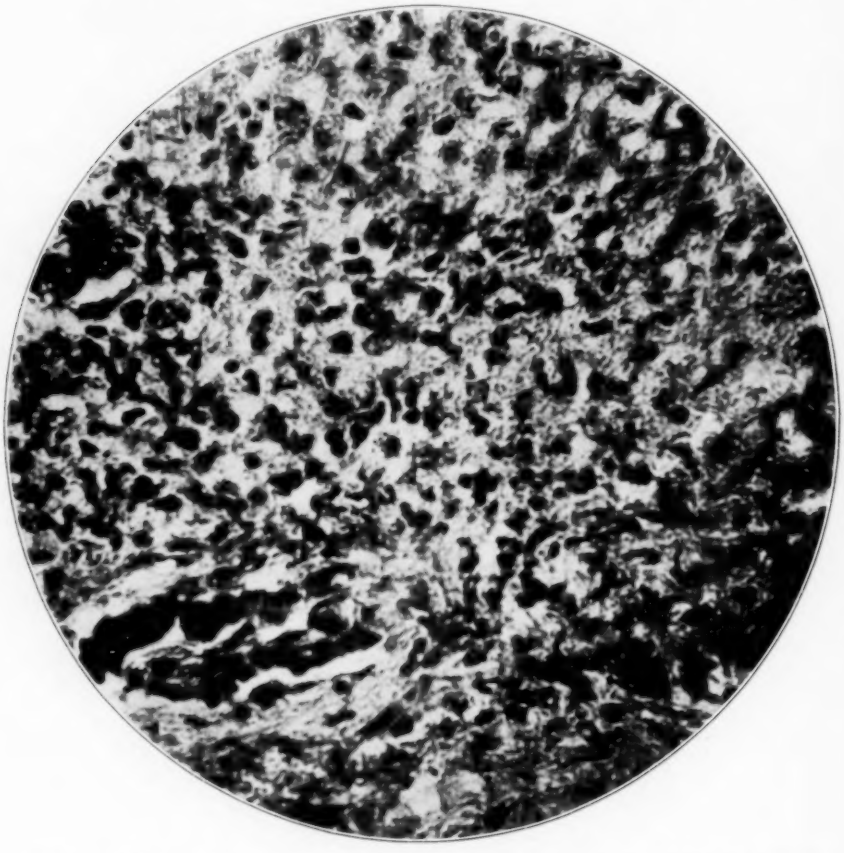

Fig. 7.—Under high power magnification the epidermis presents a very unusual picture; the entire epidermis is converted into a network in which the usual architecture of the epidermis and the normal arrangement of the cellular element is lost. Note the naked nuclei lying nested in cavities made by the cell bodies after the disappearance of the cytoplasm.

cytes, connective tissue cells and polymorphonuclear leukocytes as an infiltration (perivascular) or collaret about the vessels. New blood vessels were also present. The picture was that of granulation tissue. No tubercles were seen. Though a few plasma cells were noted, they were not in a direct relation to the vessel wall. In other words, there was granulation tissue in the subcutis, an acute necrosis in the cutis and an acute rupture and tearing of the epidermis from the cutis below.

Lichenoid Papule: In the section shown in figures 6 and 7, the process was limited to the middle and upper cutis. In places the dividing line between the epidermis and cutis was lost. The characteristic features were: (1) moderate dilatation of the vessels with a mild cellular infiltration extending up to and including the epidermis; (2) considerable interstitial edema of portions of the epidermis together with some parakeratosis, e. g., some scales. The high power lens revealed an infiltration of the cutis. It was composed of round cells and connec-

Fig. 8.—Low power magnification of a crusted papule. In the portion covered by the hemorrhagic crust the epidermis is completely wanting and the tissue underneath shows considerable edema.

tive tissue cells. Similar cells were seen in the epidermis. The epidermis presented an unusual picture. The entire affected epidermis was converted into a network in which the usual architecture of the epidermis and the normal arrangement of the cellular element were lost. There was present only the outline of the cell bodies with naked nuclei lying nested in cavities made by the cell bodies after disappearance of the cytoplasm. It was an unusual picture which has never been described before.

Crusted Papule: This section showed the same general picture. In the portion covered by the hemorrhagic crust the epidermis was completely wanting in places which were filled in by coagulated blood, serum and fibrin (figs. 8 and 9). The tissue immediately underneath showed considerable edema. In the midcutis there was a cellular infiltration about the vessels. There was present a different cellular infiltration in the eroded portion from that on each side, where the epidermis was still intact. The cellular infiltration was limited to the upper cutis. The infiltration was made up of lymphocytes and polymorphonuclear leukocytes. The vessels in

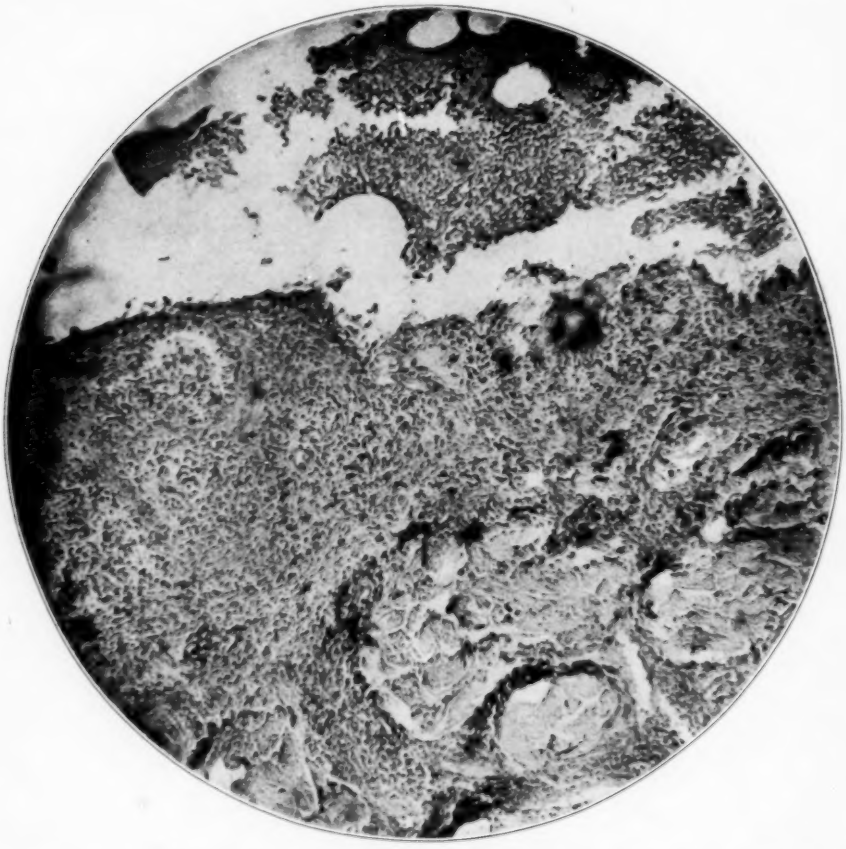

Fig. 9.—High power magnification reveals that the crust consists of coagulated blood, serum and fibrin.

the region in which the epidermis was intact were slightly dilated. The others were considerably dilated and filled with blood.

Treatment.—Since there is no specific therapy for this dermatosis, and since the various measures that have been recommended have not always been effective nor can one be certain, in a self-limiting disorder, such as pityriasis lichenoides et varioliformis apparently proves to be in some instances, that the treatment employed was responsible for the involution of the lesions, I decided to try sodium gold thiosulphate empirically in doses varying from 25 to 50 mg. (0.025 to

0.050 Gm.). Six intravenous injections were given at intervals of three days without any noticeable change in the eruption. Up to the present writing the patient is taking, while on board his ship, 5 drops of a solution of potassium arsenite three times a day after meals. This medicament is, also, apparently ineffective. I shall try the other remedies suggested for this condition in turn with the hope of obtaining results.

SUMMARY

A middle-aged seaman presented on the covered portions of his body an unusual eruption characterized by the occurrence of macular, papular, vesicular, hemorrhagic and necrotic lesions, which appeared in crops, exhibited various stages of development, ranging from macule to varioliform scars, were unaccompanied by subjective sensations, favored the flexor surfaces of the extremities and the anterior aspects of the trunk and were still actively progressive after a lapse of two years.

The histologic changes varied with the stage of development of the lesion. Thus, the early lesion (macule) presented the picture of granulation tissue in the subcutis, acute necrosis in the cutis and a tearing of the epidermis from the cutis below. The papule showed a loss of the dividing line between the epidermis and cutis, a loss of the usual architecture and parakeratosis of the epidermis and a cellular infiltration of the epidermis, upper and middle cutis. The crusted papule was characterized by a loss of epidermis, by the filling up of the gap with coagulated blood, serum and fibrin, by edema and a perivascular infiltration (consisting of lymphocytes and leukocytes) in the cutis.

Since the pathologic changes enumerated are never seen in parapsoriasis, I believe that pityriasis lichenoides et varioliformis should not be grouped with the former condition.

In this case the eruption had occurred at varying intervals for over two years. Consequently, Habermann's descriptive adjective, "acuta," is not always applicable.

The therapy instituted did not influence the eruption.

NOTE.—Since this report was submitted, the patient has received ten exposures to the air-cooled alpine lamp. Each exposure was given for fifteen minutes to the front, the back and the sides at a distance of 15 inches. The eruption disappeared entirely. As far as I know now (four months later), it has not returned.

19 East Ninety-Eighth Street.

THE SENEAR-USHER SYNDROME

A DERMATOSIS COMBINING FEATURES OF LUPUS ERYTHEMATOSUS AND PEMPHIGUS *

ROBERT LOUIS GILMAN, M.D.
Assistant, Laboratory of Dermatological Research
PHILADELPHIA

In 1926, Senear and Usher [1] published their report of "An Unusual Type of Pemphigus," which included a discussion of eleven cases of a hitherto undescribed clinical syndrome. Briefly, according to the authors' description, the clinical picture embraces features of both lupus erythematosus and pemphigus. The manifestations of the former disease involve the scalp and face, either with typical discoid patches and "carpet-tack" scales, or with an inflammatory reaction suggesting a severely congested seborrheic dermatitis. The lesions of pemphigus occur on the trunk, usually in the seborrheic areas, and consist of flaccid bullae that rupture readily and develop into areas of crusted, oozing dermatitis or into an inflammatory papule with a thick, greasy or even keratotic scale and crust. The lesions usually involute spontaneously and leave pigmented patches. The symptoms are mild; itching may occur, but the course is usually relatively benign. The cases in the original Senear-Usher group were equally divided between the sexes, the age was usually the fourth or fifth decade, and the average duration when first seen was three and one-fourth years. There was a fatal outcome in only one instance.

The following thirteen cases have been presented or reported at meetings of various American dermatologic societies from 1925 to 1929. No examples were found in the foreign literature, although it is possible that such cases have received comment elsewhere.

REPORTS OF PREVIOUS CASES

CASE 1.—In the discussion of Senear and Usher's original communication, Wise,[2] of New York, reported the case of a woman, aged 45, who had an indubitable case of lupus erythematosus of the face (confirmed by biopsy), the duration of which was not stated, and who subsequently had pemphigoid lesions on the trunk. Wise considered this case one of lupus erythematosus falling in the Senear-Usher group.

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* Submitted for publication, Dec. 3, 1930.

* From the Hospital of the University of Pennsylvania and the Laboratory of Dermatological Research, University of Pennsylvania School of Medicine.

1. Senear, F. E., and Usher, B.: An Unusual Type of Pemphigus, Arch. Dermat. & Syph. **13**:761 (June) 1926.

2. Wise, F., in discussion of Senear and Usher (footnote 1, p. 781).

CASE 2.—Walzer [3] presented a man, aged 41, who had had a dermatosis for six months. There were extensive bullous lesions of the body; the scalp was free. Nikolsky's sign was absent. In the discussion that followed, Wise suggested that the case represented a combination of seborrheic eczema and benign pemphigus similar to those reported by Senear.

CASE 3.—At a meeting of the Chicago Dermatological Society, Senear [4] presented a woman, aged 64, who showed bullae and keratotic lesions of the trunk closely associated with trauma. Subsequently,[5] the patient presented a typical picture of lupus erythematosus on the face with flaccid bullae and crusted lesions on the trunk. Death resulted from septicemia.

CASE 4.—Schamberg [6] reported the case of a young woman who had a disseminated type of lupus erythematosus associated with pemphigus-like bullae of the trunk. The white blood count was 3,500. The condition was rapidly fatal.

CASE 5.—Among a series of cases of lupus erythematosus presented at a meeting of the Minnesota Dermatological Society, O'Leary and Goeckerman [7] presented a case of the Senear type of fifteen months' duration in a woman, aged 35. The onset occurred about the eyelids, and the first complaint was photophobia. The face was subsequently involved in a process resembling lupus erythematosus, without plugging but with telangiectasia and atrophy. Nikolsky's sign, the blood count and pruritus were not mentioned. The mucous membranes, the chest, the arms and the genitalia were involved.

CASE 6.—Valade [8] presented and later reported [9] a case of lupus erythematosus with features of dermatitis herpetiformis in a Negress, aged 55. The duration was six months. The condition was typical of lupus erythematosus of the face with associated pruritic papulovesicular lesions of the body. The scalp was not involved. Subsequently, bullae developed, and Nikolsky's sign was present.

CASE 7.—Grindon [5] presented a woman, aged 55, who had been under treatment for five years. Reddish patches had appeared on her abdomen seven years previously and had spread to the face and chest. Subsequently, bullae had developed on the trunk, followed by yellow crusts and scales. The original biopsy showed lupus erythematosus, but subsequently the case clinically suggested pemphigus foliaceus.

CASE 8.—In the discussion of Grindon's patient, Davis [10] reported a case of apparent disseminated lupus erythematosus in a woman. The patient recovered from a septicemic condition, but died of what appeared to be an acute septic pemphigus.

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3. Walzer, A.: Pemphigus, Arch. Dermat. & Syph. **13**:445 (March) 1926.
4. Senear, F. E.: Pemphigus, Arch. Dermat. & Syph. **13**:552 (April) 1926.
5. Grindon, J.: Unusual Form of Pemphigus Combining Features of Lupus Erythematosus (Senear), Arch. Dermat. & Syph. **18**:463 (Sept.) 1928.
6. Schamberg, J. F.: Lupus Erythematosus, Arch. Dermat. & Syph. **14**:228 (Aug.) 1926.
7. O'Leary, P. A., and Goeckerman, W. H.: Chronic Lupus Erythematosus Disseminatus (Lupus Erythematosus—Pemphigus Syndrome of Ormsby and Senear), Arch. Dermat. & Syph. **15**:92 (Jan.) 1927.
8. Valade, C. K.: A Case for Diagnosis, Arch. Dermat. & Syph. **16**:246 (Aug.) 1927.
9. Valade, C. K.: Report of a Case of Lupus Erythematosus in a Negress, J. Michigan M. Soc. **26**:356 (June) 1927.
10. Davis, R. H., in discussion of Grindon (footnote 5, p. 464).

Case 9.—In Cleveland, Fisher [11] showed a man, aged 29, who for the previous fifteen months had had erythematosus vesicles on the face, the trunk and the arms. The buccal mucosa was involved. In the discussion that followed, O. H. Foerster suggested that the case belonged in the Senear group. Ormsby termed the case one of atypical pemphigus with lupus erythematosus and features of seborrheic dermatitis.

Case 10.—Grau and Pelaez [12] presented a man, aged 48, at a meeting of the Cuba Dermatological Society. Seven months previously the patient had had what appeared to be a seborrheic dermatitis behind the ears, which progressed to the

Fig. 1.—Alopecia and involvement of the face and crusted lesions over the thorax.

scalp, the face and the body. Bullae were found later, and Nikolsky's sign was present. The blood count was normal.

Case 11.—Cole and Driver [13] presented a boy, aged 7, who had had an involvement of the face and external genitalia with bullae for two and one-half years.

11. Fisher, J.: Pemphigus Resembling Lupus Erythematosus, Arch. Dermat. & Syph. **18**:942 (Dec.) 1928.

12. Grau and Pelaez: Chronic Pemphigus, Arch. Dermat. & Syph. **19**:823 (May) 1929.

13. Cole, H. N., and Driver, J. R.: Pemphigus (Senear Type?), Arch. Dermat. & Syph. **20**:140 (July) 1929.

Examination of the blood gave negative results. The case was presented as a case of the Senear type, to which Barney agreed. During the discussion, the use of gold compounds in this type of case was commented on. Both Fisher and Cole recalled experiences with gold compounds in this respect, but without unequivocal results.

CASE 12.—At the Ann Arbor meeting of the Chicago Dermatological Society, Wile [14] presented a woman, aged 34, who showed lupus erythematosus of the nose with "carpet-tack" scales. There were keratotic lesions and vesicles on the body. Nikolsky's sign and pruritus were present. The duration of the condition was not mentioned. In addition, the patient gave a Wassermann reaction of 4 plus. The case was presented as a member of the Senear group, to which classification Wieder assented. Eller suggested the diagnosis of lupus erythematosus, while O. H. Foerster termed the condition benign pemphigus foliaceus.

CASE 13.—At St. Louis, Snider [15] presented a woman, aged 51, who for the past two years had had lupus erythematosus of the face with bullae on the neck and arms. A diagnosis of Senear's lupus erythematosus pemphigoides was suggested.

AUTHOR'S CASE

History.—T. H., a very dark-skinned colored woman, married, aged 49, was first seen on Dec. 12, 1929, because of a generalized eruption associated with itching. No facts could be elicited about the family history. The patient's husband was living, but for the past four or five years had been a semi-invalid with paralysis. The patient had had three miscarriages; one child was living and well, and six children were dead from various vague causes. For the past two or three years she had had a marked arterial hypertension and had received varied treatment for this condition at various dispensaries. The diet had always been high in carbohydrates, although this tendency had been somewhat reduced recently. With the exception of the itching, she had felt in fairly good health.

The eruption of the skin had started eighteen months previously. The first symptom that she had noticed was a "pimple" on the nose that gradually spread and involved both cheeks and the bridge of the nose. Following this condition there had appeared at regular intervals a bulla on her breast and back. Each lesion subsequently became elevated and crusted. Two months following the onset of the eruption, the scalp had become involved, according to her description, a vesicular and pustular expression, and she had lost her hair rapidly. The eruption on the face spread by contiguity so that the entire nose and both cheeks were involved. The eruption in the scalp progressed posteriorly and along the sides, and the skin became raised, pigmented, crusted and finally keratotic. Coincident with the spreading of the condition on the face, more and more bullae appeared on the body and were succeeded by crusted and keratotic papules on the trunk. Itching was present almost from the onset, and with the exception of a period of transient relief following the administration of three intravenous injections of an unknown medicine during August and September, the condition had slowly progressed. The only other previous treatment that she recalled was the use of some patent sulphur pills.

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14. Wile, U. J.: A Case for Diagnosis, Arch. Dermat. & Syph. **20**:536 (Oct.) 1929.

15. Snider, M. C.: Case for Diagnosis, Arch. Dermat. & Syph. **20**:558 (Oct.) 1929.

The Cutaneous Condition.—The scalp was almost bald, particularly over the anterior portion and the sides (the patient wore a wig) and was covered with a black, almost verrucous, crust. No individual lesions could be made out in the scalp. Continuous with this process, but exempting the forehead, were a thickening and hypertrophy of the skin over the nose and both cheeks (butterfly pattern) and extending to both ears. Small "carpet-tack" scales were easily removed from that portion of the cheek nearest the nose, and although the follicles were generally dilated, no plugs were found. The race of the patient and the deep pigmentation

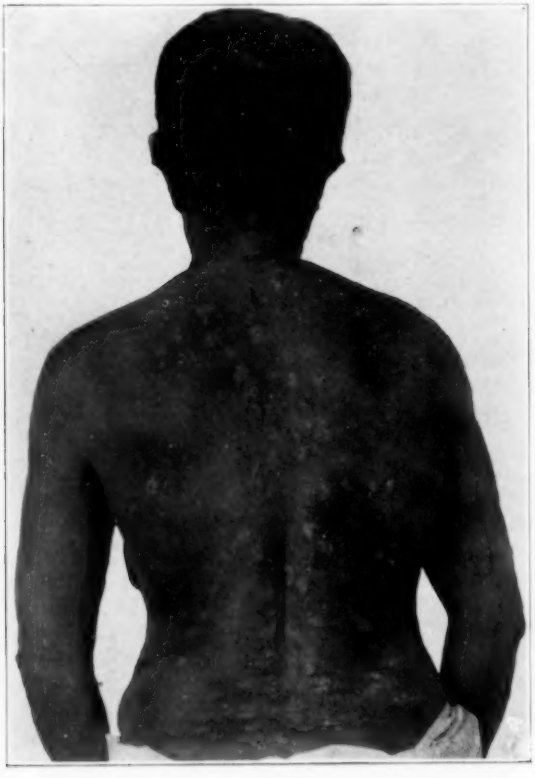

Fig. 2.—The characteristic crusted and keratotic lesions over the back. (The patient had retained her wig.)

may have been responsible for the failure to see any evidence of telangiectasia. Such atrophy as existed was confined to the scalp.

Over the trunk, especially on the chest and back, were many scattered, isolated and grouped, flat and crusted, oval and round papules, ranging from 1 to 1.5 cm. in diameter. These papules were definitely elevated and infiltrated and were covered with a thick greasy crust. The tendency of the papules to group in circular patterns was striking. Over the back, where the lesions were particularly numerous, there were a dozen or more lesions that were verrucose if not actually fungating. In this region there was a tendency for the papules to follow roughly the natural lines of cleavage. Over the sacrum and the lower right quadrant of

the abdomen there were several isolated, ruptured, bullous lesions. Three or four small vesicles were seen in the region of the left breast. The left palm showed signs of a recent exfoliative process, but no signs of present activity. The other palm and both soles were normal on examination. Although there were some crusted papular lesions on the upper part of the arms and to a less extent on the thighs, there were practically none below either the elbows or the knees. The mucous membranes of the mouth were uninvolved, and the axillae, the anus and the genitalia were free from lesions. Nikolsky's sign was not present.

Laboratory Studies.—Examination of the blood, made on the day of admission, showed: hemoglobin, 60 per cent; red cells, 2,960,000; white cells, 2,850; differen-

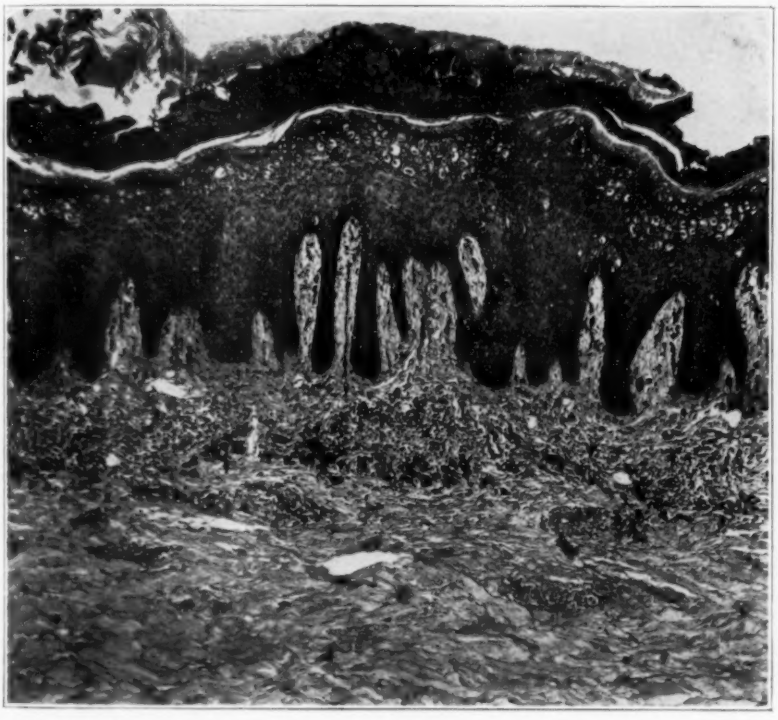

Fig. 3.—Photomicrograph of a section of skin from the abdomen. Cluster of chromatophores in the center of the subpapillary region. Extreme hydrops of the stratum granulosum (seat of future formation of blebs?); × 72.

tial count: polymorphonuclears, 55 per cent; large monocytes, 4 per cent; lymphocytes, 40 per cent; eosinophils, 1 per cent. The Kolmer modification of the Wassermann test and the Kahn test gave negative results. Four days later the white cell count was 5,700. A specimen of blood sent to Dr. Isaac Pels for a Pels-Macht [16] determination was reported as 54 per cent. This result is com

16. Pels, I. R., and Macht, D. I.: Phytopharmacologic Examination of the Blood in Pemphigus and in Some Other Diseases of the Skin, Arch. Dermat. & Syph. **19**:640 (April) 1929.

parable to the average of 53.8 per cent obtained by Pels and Macht in pemphigus. A subsequent specimen taken two weeks later gave a reading of 52 per cent. A third determination was reported as 57 per cent.

Histologic Observations.—Material for biopsy study was taken from a crusted lesion on the lower right part of the abdomen and from the edge of the process in the right cheek. Dr. Fred D. Weidman reported as follows:

In the section from the abdomen, the picture was that of a subacute diffuse dermatitis, without expressing any peculiarities or specialties that would designate the process as either pemphigus or lupus erythematosus. The particular form which the reaction in the corium took was that of the commonplace infiltration of

Fig. 4.—Photomicrograph of a lesion of the face. Atrophy of the epiderm and moderate dilatation of the follicles of the hair. Infiltration of round cells in the corium is sparse at this stage of the lesion; × 72.

round cells (lymphocytic) around the blood vessels and edema. Polymorphonuclears were scarce. The only other feature in the corium deserving special note was the large number and size of the chromatophores in the subpapillary parts. The chromatophores were extraordinarily highly developed, even for a very black Negress.

In the epiderm the acanthosis was of an extremely high grade, the expressions in the stratum corneum being those of simple hyperkeratosis in some places and of parakeratosis in others. The only feature that was extraordinary was the form taken by the keratosing phases in the stratum granulosum. Thus, instead of the cell being narrow and its cytoplasm crowded with blue-staining granules, it was

for the most part hugely swollen and fused with its neighbors, and the granules in the cytoplasm were exceedingly minute and took the basic dye. Many cells contained, in addition, a large number of more or less coalescing vacuoles, which gave a reticulated effect to the cytoplasm; this effect was so extreme that at times the nucleus appeared to lie in a lake traversed by only a few shreddy, blue remnants of the cytoplasm. The nucleus was of the pyknotic type usual to such cells, but the mode of distribution of the granules in the cytoplasm made one wonder whether the nuclear substance was not the seat of liquefaction or other

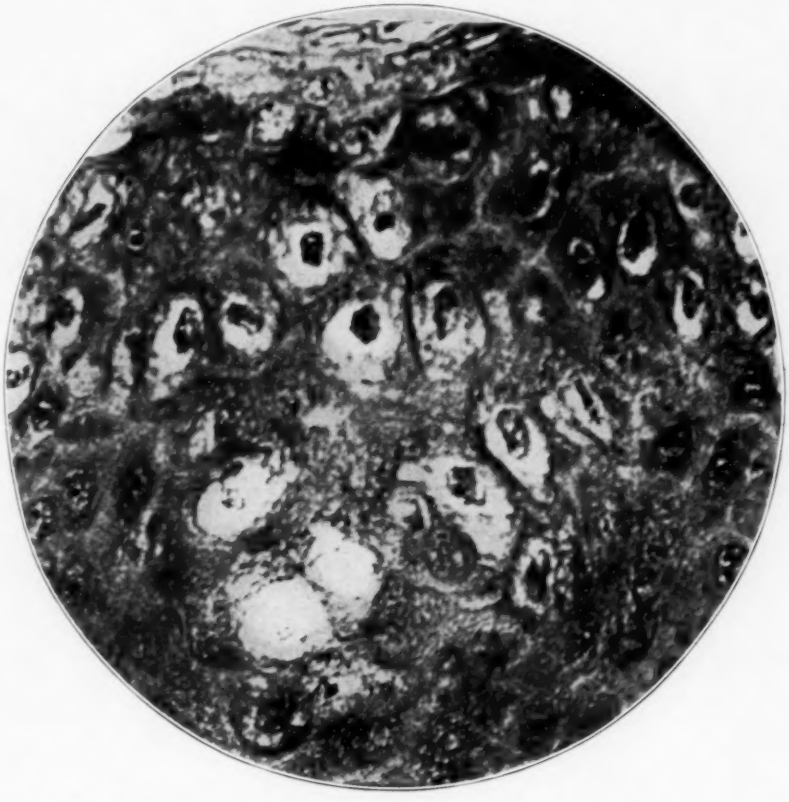

Fig. 5.—Photomicrograph showing the details of the hydropic or mucoid changes in the stratum granulosum. The hazy effect, which suggests an uncritical focusing, is due to degenerative changes; × 726.

transformations whereby it became dispersed into the cytoplasmic substance. This observation is in accordance with the idea of the formation of mucin (derived from the nucleus) as set forth by Adami. All of the components of these cells were poorly defined, as though they were degenerate.

The section from the face conformed with that from the abdomen only with respect to the type of cells and pigment that infiltrated the subpapillary region. Elsewhere the features were compatible with an atrophic phase of lupus erythematosus; but the section itself was not diagnostic of that condition. Thus, in places there was an extreme atrophy of the epiderm; only one or two layers of cells

acted as the covering. Some of the pilosebaceous orifices were dilated and plugged with keratinous débris, but the effect was far removed from the extreme comedo formation of classic lupus erythematosus.

Summary.—The processes in the specimen from the abdomen should be regarded as more acute than those in the specimen from the face. Besides inducing the trite acanthosis, the skin reacted against the noxae in the case by inducing a rather high grade of perivascular reaction such as is common to many dermatoses. The process of keratinization proceeded differently from the usual course either of keratosis or of parakeratosis; perhaps it was merely a vagary of water metabolism resulting in a hydrops or mucoid degeneration of the stratum granulosum which was responsible for the unusual observations.

It might be difficult to reconcile the epidermal changes of the abdomen and the lesions of the face (extreme hyperplastic changes of the former and the atrophy of the latter) until one recalls the differing pictures in the acute and chronic stages of other atrophic dermatoses. Allowing eight or nine months for the evolution of the acute processes, the changes in the lesion of the face become understandable.

White Cell Counts Taken at Each Visit

Date	White Cell Count	Date	White Cell Count
December 16	5,700	January 16	6,800
December 19	5,400	February 4	6,400
December 24	9,200	February 11	5,800
December 31	9,200	February 18	6,600
January 7	7,800	March 4	6,800

In any event, the picture of the lesion of the face was not that of classic lupus erythematosus; the degree of infiltration of round cells was not sufficient, nor did the infiltration extend in the massive tractlike form that ought to be expected even in the atrophic phases of this disease. The degree of dilatation of pilosebaceous orifices was not greater than might reasonably be expected in persons with sebaceous skin and with large pores.

Pathologic Diagnosis.—The following diagnosis was made: subacute diffuse dermatitis; dyskeratosis; atrophy of the epiderm; chromatophorosis; follicular dilatation.

Clinical Course.—Active treatment was instituted on the patient's second visit to the department. Because the evidence pointed to the predominance of the features of lupus erythematosus, an initial dose of gold sodium thiosulphate was given intravenously. Frequent cleansing baths were prescribed for the lesions of the body, together with the use of a mild tar ointment. The gold salt was given at weekly intervals, and a white cell count of the blood was taken at each visit.

During treatment the clinical course was satisfactory. The pruritus was relieved early, and the patient commented on a feeling of well-being. The lesions on the body underwent involution gradually but slowly, and the most striking change had been the noticeable process of depigmentation, not only on the butterfly lesion of the face, but on the surrounding "normal" skin as well. The coexisting hypertension constituted no bar to the treatment and no consistent change was noted.

ANALYSIS OF CASES

Following Senear and Usher's exposition, the fact has been brought to light that this combination of symptoms is not a rare occurrence. There appears to be a toxic, or at least an abnormal, metabolic state that occasionally induces synchronously the morbid changes of at least two, and possibly three, different dermatologic complexes: lupus erythematosus, pemphigus and possibly seborrheic dermatitis.

A systematic and tabulated analysis of my fourteen collected cases brings out data that confirm the conclusions of Senear and Usher. It is conceded that some cases (cases 1, 4 and 8) might not belong in the group, because only occasional bullae were present to complicate an otherwise clearcut case of lupus erythematosus. However, I believe that the Senear-Usher syndrome is comprehensive enough to include such cases as these within its scope, despite the clinical predominance of one feature. Leukopenia, Nikolsky's sign, the Pels-Macht determination and biopsy may serve as diagnostic criteria. However, in the analysis of general symptomatology that follows, the three cases will be omitted.

The eleven cases remaining occurred in four men and seven women. With the exception of the case reported by Cole and Driver in a boy of 7, the age incidence is mainly the fifth and sixth decade. In the cases reported, the duration of the condition up to the time of presentation ranged from six months to two and one-half years. The average duration was thirteen months. Two of the cases occurred in colored women.

In nine cases specific mention was made of the involvement of the face or the scalp. The type of lesion ranged from seborrheic dermatitis through the gradient forms to typical lupus erythematosus. The lesions on the body were mainly located on the trunk; they varied between bullae and crusted keratotic papules. Two cases included bullous lesions about the genitalia; one showed in addition involvement of the mucous membranes of the mouth. A third patient had lesions in the mouth without genital lesions. In three cases pruritus was a prominent symptom, and in two a tendency of the lesions of the trunk to group in circles was noted. Nikolsky's sign was positive in three cases and not mentioned in four. All of the eleven cases displayed evidences of changes and remissions. With the exception of case 8, the course though evidently chronic appeared benign in comparison with the course of the usual case of pemphigus or of acute lupus erythematosus disseminatus.

PATHOLOGIC FACTORS

Of the three outstanding phases of the syndrome under consideration (lupus erythematosus disseminatus, pemphigus and seborrheic dermatitis), it is not surprising that the first two occur in a general toxic state. The pathologic factors of these diseases are already sufficiently covered

in the dermatologic literature. Turning to seborrheic dermatitis, it becomes necessary to consider what the presence of this supposedly exogenous dermatosis indicates in the company of the other two; this is the interesting pathologic phase of the entire subject.

The histologic observations show little more than one would expect in lesions with the clinical appearance of lupus and pemphigus. In Senear and Usher's original communication, the histologic observations were not recorded in a form that facilitated appraisal of tissue processes that were distinctive of an entity. However, their case 1 was accompanied by excellent photomicrographs that located the definite vesicular changes in the prickle cell layer of the epiderm. The pertinent features in case 3 were Finnerud's observation of vacuolar degeneration of the epiderm and slight parakeratosis.

The two histologic observations that have appeared subsequent to the publication of Senear and Usher's paper were those of Wise (case 1 of my series) and Grindon (case 7), in both of which characteristic lupus erythematosus was reported. That is, the histologic changes were of the order that would be expected from the clinical characters (pemphigus, lupus erythematosus and seborrheic dermatitis) without the addition of any constructive element. As to my own case, there was an early or premature formation of blebs due to hydropic changes that occurred even higher up in the epiderm than those in the other cases accompanied by a moderate amount of cellular infiltration in the corium. Excepting the occurrence of this infiltration, the primary changes were preeminently epidermal and on the whole comparable to the previously recorded histologic observations.

As to the aspect of "seborrheic dermatitis," the solitary histologic observation on this point (Senear and Usher's case 9) went no farther than to corroborate the clinical impressions. At this point information is particularly needed: Given a seborrheic distribution clinically, and the superficial erythematous infiltration that accompanies this dermatosis, are the hypersebaceous anatomic and physiologic features present that are fundamentally necessary for the concept of seborrheic dermatitis? Or is one deceived by some caprice of cutaneous pathologic changes whereby seborrheic areas are elected for disturbance without the sebaceous glands being incriminated? It is difficult to understand how the latter condition could occur; nevertheless, future pathologic studies should include examination for possible fatty changes in the sebaceous areas of dermatitis by means of frozen sections and specific stains for fat. Does the clinical distribution really connote the involvement of (1) sebaceous glands, quantitatively, (2) their fat metabolism qualitatively or (3) sweat glands (which also secrete fat, although in very small quantities)? To this, analysis of surface fats might well be added.

In connection with the second point, it is felt that dermatologists have long neglected the possibility that the occurrence of abnormal fats in sebaceous secretion might be a weighty factor in provoking abnormal epidermal physiologic conditions (in my case the hydropic changes in the epiderm might well be interpreted as metabolic); the rôle of cholesterol in decreasing surface tension is already established. Cholin, with a toxicity of the order of muscarine, is another lipoid substance related to lecithin, but its presence in the skin remains to be shown. However, if such a substance could be shown in the Senear-Usher syndrome, it would fill a gap in the understanding of the pathology of this syndrome.

Incidentally, the occurrence of precocious calcification in Senear and Usher's original patient (a woman, aged 24), while not convincing, would be in keeping with a state of faulty metabolism of fat, since fatty accumulations predispose to calcification.

On the other hand, the mechanism of the genesis of the seborrheic dermatitis may be the reverse; this mechanism is simple; namely, the essential toxic pemphigoid state stimulates the sebaceous glands to the extent that (a secondary) seborrheic dermatitis makes its appearance, even though this condition does not occur as part of conventional pemphigus or lupus.

This explanation would be the easy way out of this problem in pathology, but at the same time is no reason why inquiries into the truth should not be made, even though the way be more difficult. In this problem there is the old vis-a-vis: Is the seborrheic dermatitis in the case one of the primary factors or is it secondary?

DIFFERENTIAL DIAGNOSIS

As in Senear and Usher's original group, my case and those previously abstracted fall in a limited category of diagnostic possibilities: (1) a combination of various grades of seborrheic dermatitis or lupus erythematosus with the additional clinical signs of pemphigus, (2) dermatitis herpetiformis or (3) a chronic form of erythema multiforme.

As an example of the various features possible in a single patient, I may state that after the presentation of my patient at a meeting of the Philadelphia Dermatological Society,[17] it was suggested by various physicians that the case was one of seborrheic eczema, persistent erythema multiforme and lupus erythematosus with disseminated papular lesions of the trunk.

Other diagnoses cited and dismissed by Senear and Usher, such as impetigo and epidermolysis bullosa need not be discussed. While it is

17. Gilman, R. L.: Atypical Benign Pemphigus (with Features of Lupus Erythematosus as Described by Senear and Usher), Arch. Dermat. & Syph. **21**: 1078 (June) 1930.

possible to be didactic and to denominate each of the eleven cases as a single clinical entity, the alternative, namely, to say that all of them are lupus erythematosus with added features of pemphigus, is justified because the combination of symptoms has occurred so often; that is, such a frequent combination has significance and is not coincidental.

The order of pathologic basis is the same in dermatitis herpetiformis as in the Senear-Usher syndrome. The condition is doubtlessly toxic; the same may be said of the third alternative, namely, chronic erythema multiforme. After this, however, the clinical phase offers one further information and enables one to refine the diagnosis. Any dermatologist can apply such criteria as the extreme itchiness, the grouping of lesions, etc., of dermatitis herpetiformis and the differing distribution of chronic erythema multiforme.

The clinical distinctions are still of service, even though the exciting etiologic factor is the same. The following hypothesis cited by Senear challenges serious consideration:

> A group of toxic eruptions exists, including pemphigus, lupus erythematosus, erythema multiforme and other toxic erythemas, dermatitis herpetiformis, urticaria, etc., the members of which are closely allied from the etiologic standpoint, and . . . that a single toxic agent may produce one of these diseases in one person and another of these conditions in a second person, or that it may produce more than one of these conditions in one person at different times.

However, it is still possible that this or that particular syndrome in connection with a single etiologic factor may some day become valuable in identifying the particular constitutional trait (in a given patient) that is determining the particular clinical expression.

The benign aspect of this apparent combination appears directly related in this instance to the histologic evidence of the capacity of the inflammatory reaction to recede not only in the part involved by lupus erythematosus but likewise in the pemphigus lesions. This observation might likewise be interpreted as further evidence of a common toxic and lesional interrelation between bona fide examples of lupus erythematosus and pemphigus. Another bond in support of the common toxic change may be the Pels-Macht phytopharmacologic test, although thus far sufficient data have not been collected on typical examples of lupus erythematosus, either of the discoid or of the acute disseminated variety.

For several years Ormsby [18] has recognized a comparatively benign form of pemphigus with certain features of lupus erythematosus which, because of further observations and the histologic studies of Finnerud, has caused him to place it provisionally with the pemphigus group.

It is now granted that Duhring, in recognizing and creating an approved entity in dermatitis herpetiformis, reversed the habit of the

18. Ormsby, O. H.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1927, p. 305.

many previous authors of isolated reports of "a new and hitherto undescribed vesicular eruption" and was able to synthesize a number of previous nondescript dermatologic conditions into a logical and necessary classification. Similarly, the creation and insistence of the Senear-Usher concept of the cases described will be useful and will serve as a midway station, or, as the original authors suggested, a state of toxic eruption transitional between lupus erythematosus disseminatus and pemphigus. The recognition of this syndrome should not add further complexities, but rather should clarify and aid in the necessary elasticity needed in clinical diagnosis.

TREATMENT

The most successful type of treatment appears to be indicated by that part of the clinical picture which predominates. The remissions and clinical changes possible during the course may make it advisable to change from a therapeutic management of lupus erythematosus to any of the accepted types of therapy employed in pemphigus. The use of a gold compound on my part was indicated by the clinical status of the features of lupus erythematosus, that is, by a decreased white cell count and by the absence of indubitable features of pemphigus other than those suggested by the Pels-Macht determination.

CONCLUSION

1. Thirteen cases taken from society transactions are discussed; in these cases there is a combination of features of both lupus erythematosus and pemphigus.

2. An additional case is reported in detail; it is the second reported instance occurring in the colored race.

3. Eleven of the fourteen cases seem to fulfil the postulates of the Senear and Usher syndrome.

4. The occurrence of these cases strengthens the position of the Senear and Usher syndrome as a distinct clinical entity. The syndrome represents a toxic dermatosis midway between lupus erythematosus disseminatus and pemphigus, occurring in middle-aged persons and having a comparatively benign course.

1930 Chestnut Street.

TUBERCULOSIS FROM DIRECT INOCULATION WITH AUTOPSY KNIFE

REPORT OF A CASE *

HARRY E. ALDERSON, M.D.
Clinical Professor of Medicine (Dermatology), Stanford School of Medicine
SAN FRANCISCO

The date of accidental inoculation and the course of events in this case being definitely known, it is felt that a report would be of interest.

CASE REPORT

An intern, aged 25, while assisting at an autopsy on a patient with tuberculosis on July 8, 1929, pricked his left index finger (flexor aspect) with the knife. Two weeks later, he noticed a nodule the size of a pea at the site of the injury. He incised the nodule, but there was no pus. Within a few days, painful axillary (left) adenopathy developed. The epitrochlear glands did not become involved. The axillary glands slowly enlarged, and five months later became soft and fluctuating. The primary lesion constantly remained nodular and never became verrucose or pustular, but a very small amount of serum could be readily expressed. There had been no rise in temperature.

At the time of examination, the patient's general condition was good. His past health had been good, except for questionable pulmonary tuberculosis at the age of 14, from which he recovered completely after treatment and rest for five months. The blood count showed: white cells, 9,700; polymorphonuclears, 63 per cent; lymphocytes, 33 per cent, and transitionals, 4 per cent. Agglutination tests of the blood for tularemia gave negative results.

Pus from an axillary gland showed tubercle bacilli in smears, and tuberculosis subsequently developed in the guinea-pig into which the pus was injected.

The patient was first under the care of Dr. P. H. Pierson (San Francisco), and subsequently in the Colfax School for Tuberculosis in charge of Dr. Robert A. Peers.

Jan. 6, 1930: The patient entered the hospital, and rest in bed for twenty-two and one-half hours daily was started. His weight was 158¼ pounds (72 Kg.). The temperature was below normal. His general physical condition was good. No pulmonary involvement was found. Treatments with ultraviolet light were started, being concentrated on the axilla for six minutes daily. After ten days the time out of bed was increased to two and one-half hours and a week later to three and one-half hours, with five minutes of exercise.

Jan. 29, 1930: Treatments with a lamp were augmented with sunlight, beginning with five minutes on the legs and increasing five minutes daily, the areas treated being gradually extended.

Feb. 7, 1930: The tuberculoma on the left index finger discharged thick white pus on pressure. At 2 p. m., 0.4 mg. of old tuberculin was injected into the center of the lesion on the finger. At 5 p. m., the finger was becoming increasingly swollen, red and painful and could not be flexed. There was no rise in tempera-

* Submitted for publication, Dec. 9, 1930.

ture, but the patient had general malaise, headache and insomnia. During the night, the finger became more swollen, and a large bulla filled with bloody serum appeared at the site of the injection.

Feb. 8, 1930: About 1.5 cc. of bloody fluid was obtained from the bulla, which also drained profusely all day. Lymphangitis developed, extending as far as the elbow, and the finger remained painful. The axillary sinuses discharged copiously and became increasingly tender and swollen. The temperature varied from 100.6 (7 a. m.) to 101.6 F. (8 p. m.).

Feb. 9, 1930: The inflammation of the finger began to subside, but the axilla became increasingly swollen and tender, with increased drainage. The temperature was normal, and the feeling of malaise was no longer present.

From February 10 to 28, the axillary inflammation and discharge gradually decreased, and one of the sinuses healed, leaving only one discharging. All of the axillary glands decreased slightly in size, rendering the movements of the shoulders somewhat freer. The skin of the finger became drier and desquamated, leaving a small pit at the site of the primary tuberculoma. There was a gain of 3 pounds (1.4 Kg.), and the temperature remained normal.

March 4, 1930: The finger was only slightly stiff, and only one discharging axillary sinus remained. At 2 p. m., 0.4 mg. of old tuberculin was injected into this axillary sinus. At 8 p. m., the temperature was 99 F., and there was a feeling of malaise and headache.

March 5, 1930: The axillary sinus that had healed two weeks previously opened, and the two sinuses discharged copiously a thick, bloody serum. All of the axillary glands were much enlarged; one was red and painful. Motion of the shoulder was greatly restricted. General malaise and headache were quite pronounced. The site of the tuberculoma and the remainder of the finger were red and swollen and could not be bent. At 8 p. m., the temperature was 100.6 F.

March 6, 1930: Treatments with the lamp were discontinued, and a full exposure of one hour to the sun was given. This was gradually increased to two and one-half hours, the axilla being exposed during most of the time. Over a period of weeks the time was increased, and the patient was up for seven hours daily, with ten minutes of exercise. (There was no reaction from the tuberculin.)

March 6, 1930: The drainage and soreness had increased. Another sinus from a superficial gland on the edge of the pectoralis major had opened. The finger was slightly less swollen. Malaise and headache were still present. The temperature was 99.6 F.

March 7, 1930: At 2 p. m., 0.4 mg. of old tuberculin was injected into a discharging axillary sinus (of which there were four at this time). At 6 p. m., the axilla was painful, but there was no general malaise. The temperature was 98.4 F.

March 15, 1930: The axilla was swollen, red, painful and discharging. There was no general malaise. The maximum temperature was 98.6 F.

March 16, 1930: The axilla was sore and red. The swelling had subsided and the discharge decreased. There was no general malaise. The temperature was 98.4 F.

March 20, 1930: One milligram of old tuberculin was injected into a discharging axillary sinus. A portion of this escaped from the sinus. By evening, the area was painful, red, swollen and discharging. General malaise was present. The temperature was 98.8 F.

March 21, 1930: The area was painful, red, swollen and discharging. There was general malaise. The temperature was 99.2 F.

March 22, 1930: The inflamed area was subsiding. There was no malaise. The temperature was 98.6 F.

March 27, 1930: At 2:30 p. m., 2.5 mg. of old tuberculin was injected into an axillary sinus. By 6 p. m., there were general malaise, local pain, swelling and redness. The temperature was 100.2 F. the next day. Malaise persisted for three days, with increased drainage and pain. These symptoms had subsided by March 30.

April 5, 1930: Four milligrams of old tuberculin was injected into the axillary sinuses. There was slight general malaise the next day, with considerable local swelling. The temperature was 99.4 F.

April 10, 1930: The lesion on the finger had remained sealed, with an area covered by red, thin and shiny skin. The axillary sinuses were discharging very little. Movement of the arm was free, except that the height to which it could be raised was slightly less than that of the other arm. There were three open sinuses, one having healed but remaining inflamed. There were several slightly enlarged adjacent glands, but the clavicular and cervical glands did not seem to be involved. There was no evidence of pulmonary complication. The patient's general condition was good.

Between April 11 and Sept. 24, 1930, the patient had had numerous intracutaneous injections of old tuberculin, with marked focal and constitutional reactions. The tuberculous foci were gradually subsiding. At one time after an intracutaneous injection of 75 mg. of old tuberculin the site of the primary lesion on the finger became red, swollen and painful, remaining so for three days.

At the time of writing this article, the patient's general condition was good, but he still had four discharging axillary sinuses (one having healed). He was exposing the axilla to the sun for two hours daily.

490 Post Street.

FOLLICULITIS DECALVANS AND LICHEN SPINULOSUS

REPORT OF A CASE *

EUGENE F. TRAUB, M.D.
AND
JESSE A. TOLMACH, M.D.
NEW YORK

Reports of cases presenting a curious combination of two known clinical entities, folliculitis decalvans and lichen spinulosus, are comparatively rare in the literature.

In 1915, Graham Little [1] presented a case before the Royal Society of Medicine in which both these conditions existed. His patient was a woman, aged 55, who said that her hair had been falling out in patches over a period of ten years. Five months before presentation, the patient suffered a sudden inflammation, with itching of the scalp, in which the hair came out in handfuls. At the same time, there appeared on the axillae, groins and flexors of the elbows an itchy, follicular eruption made up of grouped patches. On the back and external surfaces of the arms, there was a diffuse spiny folliculitis.

Dore [2] and Beatty [3] reported somewhat similar cases in the same year, although, as a result of histologic study, the latter was forced to regard his case as an unusual form of Darier's disease.

Two cases similar to Little's case were shown and described in 1920, one by Senear [4] and the other by Ormsby.[5] No biopsies were made in these cases, but the history and clinical appearance in both instances undoubtedly place them in the same category as Little's original case.

In 1924 and again in 1926, Graham Little [6] presented a case showing this curious coincidence. McCafferty,[7] in 1928, reported a case of fol-

*Submitted for publication, Nov. 13, 1930.

1. Little, E. G.: Folliculitis Decalvans et Atrophicans; Case Report, Brit. J. Dermat. **27**:183, 1915.

2. Dore, S. L.: Lichen Spinulosus and Folliculitis Decalvans; Case Report, Brit. J. Dermat. **27**:295, 1915.

3. Beatty, W.: Folliculitis Decalvans et Lichen Spinulosus, Brit. J. Dermat. **27**:331, 1915.

4. Senear, F. E.: Folliculitis Decalvans and Lichen Spinulosus, Arch. Dermat. & Syph. **2**:198 (Aug.) 1920.

5. Ormsby, O. S.: Case Report, Arch. Dermat. & Syph. **1**:471 (April) 1920.

6. Little, E. G.: Case Report, Brit. J. Dermat. **36**:383, 1924; Ibid. **38**:454, 1926.

7. McCafferty, L. K.: Folliculitis Decalvans et Atrophicans (Little), Arch. Dermat. & Syph. **18**:514 (Oct.) 1928.

liculitis decalvans with lichen spinulosus and in this case histologic studies made of the lesions on the scalp and of those on the body showed practically the same picture. Each showed a hyperkeratosis with the presence of horny plugs in the follicles and no evidences of "corps rond."

According to Little, Schauman and Straszberg each described a case presenting this combination of lesions on the skin. Unfortunately, however, references to these cases are not available.

The following case was observed by us at the New York Skin and Cancer Hospital, and was presented by Dr. Traub before the New York Dermatological Society in February, 1930, where the consensus favored the diagnosis given in the following report.

REPORT OF CASE

History.—A. M., aged 35, a tailor, was born in Austria. His father, who had always been in good health, died of pneumonia many years before the patient consulted us. His mother, one brother and two sisters were living and well. No one in the family had had any disease of the scalp or skin.

The patient had had no diseases other than measles and grip. He said that he had not taken drugs of any kind before the appearance of the eruption. The present trouble began about two years before with a loss of hair in small patches scattered over the scalp, particularly anteriorly. There was little inflammation or scaling at any time. From four to six months before consultation, an eruption was first noted on the body. Except for slight itching at intervals, there were no subjective symptoms.

Examination.—The patient presented numerous types of lesions on the body. On the face, there were two symmetrical patches about 2.5 cm. in diameter, located over each malar eminence and directly anterior to each ear. The only characteristic features distinguishable in these spots were the distinct atrophy and the pigmentation. On the trunk were scattered spiny and follicular lesions and also small rounded patches with clearing centers and elevated borders leaving pigmentation in their wake. Near the axillae and in the flanks there was a profuse, slightly elevated, deeply brownish-black, pigmented eruption. Some of the scattered lesions closely resembled annular lichen planus, and the pigmentation caused by these lesions was also similar.

Because the follicular eruption resembled a type of grouped lesions frequently seen in lichen scrofulosorum, this diagnosis was considered as a possibility for some time. At hardly any time during the period of observation were classic spiny lesions such as are usually found in lichen spinulosus noted; yet though this feature was not as definite as it might have been, this eruption, with its "nutmeg-grater feel," distinctly fell into this group. The Wassermann reaction of the blood was negative. For histologic study a lesion resembling lichen planus was removed from the right side of the trunk, and microscopic examination showed only chronic inflammatory tissue.

COMMENT

In all of the cases reported, there is the striking analogy of a preexisting folliculitis decalvans for from two to twenty-one years, with the sudden appearance of a new follicular eruption. The presence of the lichen planus-like lesions in this case is as yet not understood. The

histologic studies of one of these lesions were of no aid to us, and the patient refused to submit to any more biopsies. The follicular lesions were definitely hyperkeratotic, and could easily be classified as lichen spinulosus. The cicatricial spots on the scalp, together with the history of the hair falling out in patches, fit in very well with the picture of folliculitis decalvans, even though there were no signs of activity in the scalp during the period of observation.

This case is not reported with a view to establishing a relationship between folliculitis decalvans and lichen spinulosus. So far as we know, there is no indication of such a relationship, if it does exist. Our purpose is purely statistical. In not a few instances, two distinct clinical entities are found to be present in a patient at the same time. It is tempting in these cases to attempt to prove a relationship between the two conditions. When the coincidence occurs on more than one occasion, one is even more tempted to accept it as a natural one. The literature contains many reports of conditions that have appeared in conjunction with other definite entities. Unless these reports are accepted at their real value, erroneous conclusions will be drawn. Such coincidences should be regarded as purely statistical information until sufficient reports are made, and then only by comparing the total incidence with the approximate incidence of each of the entities can a definite conclusion be arrived at.

It is with the hope of stimulating closer observation in cases presenting lesions of folliculitis decalvans or of lichen spinulosus that this report is made.

114 East Fifty-Fourth Street.

30 West Fifty-Ninth Street.

SEROLOGIC TESTS FOR SYPHILIS, WITH SPECIAL REFERENCE TO TREATMENT*

A COMPARATIVE STUDY

M. B. KURTZ, M.S.
AND
ZELMA ZENTMIRE, M.S.
LANSING, MICH.

The last decade has witnessed a period of great activity in the development of serologic procedures for the detection and control of syphilis. The literature on this subject is too voluminous to warrant a complete résumé. In general, excellent agreement of methods is recorded with regard to the diagnosis [1] of syphilis, and some investigators have reported that the majority of discordant results in serologic tests occur in latent cases and in old cases in which treatment has been given.[2] From the points of view of both diagnosis and control of treatment, these methods include the complement-fixation procedures of Kolmer and the New York State Department of Health and the precipitation or flocculation tests of Hinton, Kahn, Kline, Meinicke (Meinicke-Klärungsreaktion), Müller (Müller-Ballungsreaktion), Sachs-Georgi and Vernes. None of these investigators employed all of the aforementioned methods; in fact, usually only three or four methods were included in a study.

With acceptable agreement between several serologic methods when used for diagnosis, but with discrepancies in latent and old cases in which treatment has been given, it is worth while to consider the aims of treatment and the laboratory evidence of cure. Swan [3] of Chicago held that in the early case treatment is directed toward eradication of

* Submitted for publication, Dec. 17, 1930.

* From the Michigan Department of Health.

* The clinical data and the serums were furnished through the cooperation of Dr. R. C. Lintner, until recently physician for the Michigan Reformatory, Ionia.

1. Sheplar, A. E.; Lyons, M. A., and McNeal, W. J.: Serologic Discord in Latent and Treated Syphilis, Arch. Dermat. & Syph. **18**:742 (Nov.) 1928. Miller, Thomas H.: The Kline Slide Precipitation Test for Syphilis: A Comparison with the Kolmer Modification of the Wassermann Test and the Kahn Precipitation Test, with a Clinical Evaluation in Syphilitic and Nonsyphilitic Cases, Am. J. Syph. **13**:583, 1929. Todd, Lester C.: Clinical Comparisons of Complement-Fixation and Flocculation Tests, South. M. J. **22**:1070, 1929. Austin, Hester A.: A Comparative Study of 2,000 Hinton, Kahn and Wassermann Tests, J. Lab. & Clin. Med. **15**:994, 1930.

2. Gilbert, Ruth: Standardization of the Wassermann Test: Progress Report, Am. J. Pub. Health **20**:47, 1930. Sheplar, Lyons and McNeal (footnote 1). Todd (footnote 1). Austin (footnote 1).

3. Swan, Mary H.: Some Serologic Aspects of the Treated Case of Syphilis, Am. J. Syph. **13**:216, 1929.

the infection and in the late case toward building up resistance in order to bring about an arrest. She warned against employing too strenuous treatment in an effort to produce negative reactions in the serum in a late case at the expense of breaking down toleration to medication. Concerning the laboratory evidences of cure, Todd [4] found that positive reactions to the precipitation flocculation tests persist longer in the patient under treatment than those of the Kolmer modification of the Wassermann test. In the experience of Davenport,[5] the Kahn reaction sometimes becomes negative after a short course of treatment and sometimes parallels the amount of treatment, and notably in the congenital cases its positivity is not affected by any amount of treatment. Gilman and McIntyre [6] reported that either the Kolmer or the Kahn test alone furnishes adequate serologic control during treatment. Meinicke [7] questioned whether sensitive methods are not perhaps too strong to be reliable during treatment.

EXPERIMENTAL STUDY

Because of the importance of further work concerning the reliability of serologic tests as guides in treatment and cure, such a study was made in this laboratory. Serums from 240 patients were examined with eight antigens, including the following methods: the flocculation or precipitation procedures of Hinton [8] (muscle indicator), the method of Kline [9] (sensitive and very sensitive antigen emulsions), that of Müller [10] (Müller-Ballungsreaktion) and that of Kahn [11] (standard and presumptive antigens) and also with the complement-fixation methods of the New York State Department of Health [12] (cholesterolized anti-

4. Todd (footnote 1).

5. Davenport, Kenneth M.: Clinical Value of the Kahn Reaction, J. A. M. A. **94**:1736 (May 31) 1930.

6. Gilman, Robert I., and McIntyre, Mary G.: The Response of Serologic Tests to Treatment, with Special Reference to Early Syphilis, Arch. Dermat & Syph. **22**:470 (Sept.) 1930.

7. Meinicke, Ernst: New Methods for the Diagnosis of Syphilis, Arch. Path. **8**:551 (Sept.) 1929.

8. Hinton, William H., and Stuart, Genevieve O.: Hinton Glycerol-Cholesterol Agglutination Reaction: Modification in Technic (Second Communication), J. Lab. & Clin. Med. **14**:621, 1929.

9. Kline, B. S., and Young, A. M.: A Microscopic Slide Precipitation Test for Syphilis (Second Communication), J. Lab. & Clin. Med. **13**:477, 1927. Kline, B. S.: An Antigen for Use in Serum Tests for Syphilis, ibid. **13**:588, 1928.

10. Müller, R.: Die Ballungsreaktion (M. B. R.) im Serum und im Liquor cerebrospinalis, Deutsche med. Wchnschr. **54**:1032, 1928.

11. Kahn, R. L.: The Kahn Test—A Practical Guide, Baltimore, Williams & Wilkins Company, 1928.

12. Wadsworth, Augustus B.: Standard Methods of the Division of Laboratories and Research of the New York State Department of Health, Baltimore, Williams & Wilkins Company, 1927.

gen) and the Michigan State Department of Health [13] (cholesterolized antigen). Unfortunately, the antigen for the Meinicke-Klärungsreaktion was not received in time to be used in this series. The antigens employed were secured from the laboratories in which the tests originated. The Kahn standard and presumptive antigens are employed as a routine procedure in this laboratory, though the reactions with the presumptive antigen are not reported to the physician. Several hundred examinations were made with each of the other methods before this study was carried out.

Results of Eight Antigens on Serums from Treated Patients

	Lansing, Wassermann	New York, Wassermann	Hinton	Müller	Kline		Kahn		Number of Patients
					Sensitive	Very Sensitive	Standard	Presumptive	
				Less than 1 series					
Number positive*.....	6	7	6	6	5	7	4	4	
Number doubtful†....	1	1	2	3	3	3	1	3	
Number negative‡.....	3	2	2	1	2	0	5	3	10
				Approximately 1 series					
Number positive.....	11	11	6	8	6	10	8	9	
Number doubtful.....	0	1	4	3	6	2	1	1	
Number negative.....	1	0	2	1	0	0	3	2	12
				Approximately 2 series					
Number positive.....	12	16	9	11	10	18	10	14	
Number doubtful.....	2	1	6	5	7	1	1	0	
Number negative.....	6	3	5	4	3	1	9	6	20
				Approximately 3 series					
Number positive.....	3	3	1	2	3	3	2	4	
Number doubtful.....	1	1	3	2	1	0	1	0	
Number negative.....	0	0	0	0	0	1	1	0	4
				Approximately 4 series					
Number positive.....	2	5	1	3	3	6	1	5	
Number doubtful.....	4	0	5	3	4	1	3	0	
Number negative.....	1	2	1	1	0	0	3	2	7
Total.....									53

* Positive, ++++, +++ and ++.
† Doubtful, + and ±.
‡ Negative, —.

Fifty-three of the 240 serums were from patients receiving treatment for syphilis. They were subjected to tests with the eight antigens listed, and they gave a positive reaction with at least one. The results, in connection with the amount of treatment received, are considered in the accompanying table.

All of the patients represented in the table were known to be syphilitic and had received the amount of treatment indicated. A few of the patients said that they had received treatment before entering the institution. The amount of such treatment is included in that indicated in the table. The method of treatment carried out at the Michigan

13. Young, C. C.: Laboratory Manual of the Michigan Department of Health, Lansing, Mich., State Printers, 1926.

Reformatory was similar to that employed at the Mayo Clinic. A series of treatments consisted of six doses of neoarsphenamine—the first dose, 0.45 cc.; the second, 0.6 cc.; the remaining ones, 0.9 cc.—and ten doses of thio-bismol consisting of 0.2 Gm. each. The doses of neoarsphenamine and bismuth were given simultaneously at weekly intervals. A period of rest of four weeks was allowed between series.

Two facts are to be observed from the tabulated data: 1. There is a wide variation in the results of the different procedures. The variations increase as the amount of treatment increases. Obviously, there would be a decrease in variations after sufficient therapeutic treatment had been administered to produce negative reactions in most of the serums. 2. Because of these variations, it is certain that serologic results are not trustworthy guides for treatment.

COMMENT

It appears that several of the serologic tests for syphilis have practically reached their peak of efficiency as far as diagnosis is concerned, and that in the future the important work should be directed toward the development of a test having a specificity that will aid the physician in giving the required amount of treatment.

Probably a method will never be evolved that will be perfect as an aid both in diagnosis and in treatment, at least not until the reagin causing the reaction has been discovered. Nevertheless, a few years of careful study, with the united effort of clinicians and laboratory men, would greatly enhance the possibility of approaching this goal.

We are aware of the possibility that in general patients with syphilis are undertreated rather than overtreated,[14] yet because of persistently positive serologic reactions many patients are treated beyond the tolerance[15] of the tissues of the body. We have in mind both of these groups when we say that if this paper will stimulate further studies of serologic tests in relation to the treatment for syphilis, the desired contribution will have been made.

CONCLUSIONS

It is possible that a serologic test for syphilis may be oversensitive or undersensitive when considered as a guide in therapy.

Realizing that it is important that the correct amount of treatment is given and that the position of many physicians is disadvantageous in this respect, a serious study made over a period of years should be directed toward the development of a serologic test that will have greater value in the administration of treatment.

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14. Clark, J. Bayard: Regarding the Treatment of Syphilis, Am. J. Syph. **12**:10, 1928. Sanders, L. Carl: Syphilis: A Discussion of Some of the Factors in Treatment, ibid. **12**:350, 1928. Stokes, John H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926.

15. Swan (footnote 3). Stokes (footnote 14).

MICROSCOPIC DEMONSTRATION OF RINGWORM

RESULTS OF SEVEN HUNDRED AND THIRTY-THREE EXAMINATIONS *

S. E. LIGHT, M.D.
TACOMA, WASH.

For three months I prepared specimens in solutions of potassium hydroxide at the New York Skin and Cancer Hospital and examined them microscopically for ringworm fungus. During this period (April, May and June, 1930), the frequency of ringworm in the clinics was exceeded only by that of eczema. Exactly 7,661 new patients came to the skin clinics and a diagnosis of tinea was made in 651 of the cases: this was 8.49 per cent, or approximately 1 in every 12 cases presented. Of these 651 patients, 585 were sent to the laboratory for microscopic examination of lesions.

There were many so-called "borderline" cases, i. e., cases that could not definitely be diagnosed as tinea by clinical appearance alone, yet were sufficiently suggestive of ringworm to warrant a microscopic examination. In compiling these figures, reexaminations were not included. Only the results of examinations made on the first appearance in the clinic were recorded. Mosaics were all recorded as negative, and with the exception of preparations from the scalp and beard, where spores were considered diagnostic, only those preparations were recorded as positive that showed definite, unbroken mycelial threads.

Table 2 shows an analysis of the observations in these cases. Positive lesions were found in one or more areas of the body in 173 cases, or 29.5 per cent of the patients examined. Exactly 733 body areas were examined and 180, or 24.7 per cent of these examinations, showed positive lesions.

Tinea of the scalp and beard gave the highest percentage of positive reactions; infection was demonstrated in 51.5 per cent of the suspected cases. Next in percentage was tinea of the feet. Lesions were examined in 313 cases. Many of these lesions were unsuspected by the patient or were considered the normal reaction to perspiration; of these, 36.1 per cent were positive.

Worthy of comment is the low percentage of positive lesions of the hands compared to those of the feet. Lesions of the feet were positive in 36.1 per cent, whereas similar lesions of the hands were positive in

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* From the Pathological Laboratory of the New York Skin and Cancer Hospital.

only 2.2 per cent of the examinations. In only two cases were positive lesions found on both the hands and the feet. It is apparent that much expenditures of energy on microscopic examinations of such lesions of the hands is unjustified, except for purposes of research. Williams, in 1921, suggested that these lesions belonged to the epidermophytid class,

TABLE 1.—*Ringworm in 7,661 New Dermatologic Patients*

	Number of Cases	Per Cent
Diagnosed as ringworm	651	8.5
Selected for microscopic study	585	89.8
Positive	173	29.5
Negative	412	70.5

TABLE 2.—*Observations in 733 Areas on 585 Selected Cases Examined for Ringworm Infection*

	Number of Areas Examined	Positive	Per Cent	Negative	Per Cent
Scalp and beard	66	34	51.5	32	48.5
Feet, excluding nails	313	113	36.1	200	63.9
Nails	59	12	20.3	47	79.7
Body, general	89	16	18.0	73	82.0
Hands, excluding nails	179	4	2.2	175	97.8
Axilla and groin	27	1	3.7	26	96.3
Total	733	180	24.7	553	75.3

TABLE 3.—*Observations in Fifty-Nine Selected Cases Examined for Ringworm Infection of the Nails*

	Number of Cases	Positive	Per Cent	Negative	Per Cent
Toe-nails	21	5	23.9	16	76.1
Finger-nails	38	7	18.4	31	81.6
Total	59	12	20.3	47	79.7

and recent work, especially that of Peck, tends to substantiate this conception.

Infection of the nails was demonstrated in 20.3 per cent of the examinations (table 3). These were often positive long after the condition in the skin had disappeared. Lesions of the body were positive in 18 per cent, and lesions of the groin and the axillae were positive in 3.7 per cent.

MODIFICATION OF THERAPY WITH GOLD COMPOUNDS IN LUPUS ERYTHEMATOSUS

PRELIMINARY COMMUNICATION *

SAMUEL MONASH, M.D.
AND
EUGENE F. TRAUB, M.D.
NEW YORK

During the last few years there has been a great advance in the treatment for lupus erythematosus with various gold compounds. Much has been written concerning the toxicity of these preparations, all of which have been administered by the intravenous method. Many cases have been encountered in which more than 100 intravenous injections have failed to produce cure, and others in which a few carefully given doses were followed by more or less serious reactions, exfoliating dermatitis and, in a number of instances, death. To avoid these complications, experimentation was begun to determine a method of giving this valuable group of compounds which would be equally or more efficient than the intravenous route, but which would not be as hazardous. Furthermore, it seemed to us that if the beneficial results of gold compounds in lupus erythematosus depended on their reaching the diseased areas, injection directly into the lesion should prove to be an exceedingly efficient, if not the best, method of administering the drugs. Gold compounds administered intravenously could bring only a high dilution of the drug in contact with the actual lesions. In most cases in which we have used intradermal injections, the gold compound has been introduced directly into the diseased areas, and in patients with numerous lesions the only beneficial effect noted was in the lesion into which the injection was made. However, to be certain that the effect depends on introducing the gold compound directly into the lesion, we are making intradermal injections into control areas at sites removed from the actual patches of lupus. Another question that our early cases have brought up is whether or not local treatment for the lesion combined with intravenous injections is more effective than either type of treatment alone. In one of our cases more than sixty intravenous injections failed to clear up a single discoid patch that responded readily to one intradermal injection. Would the same result have been achieved

* Submitted for publication, Dec. 2, 1930.

* From the service of Dr. Eugene F. Traub, New York Skin and Cancer Hospital.

in this particular case if the patient had not received the previous intravenous medication? This point and a great many others can be answered only after this research has been carried on for a much longer period.

A 1 per cent solution of gold and sodium thiosulphate seemed to be the concentration best fitted for the purpose. In this strength the preparation could be injected intradermally, subcutaneously or into the submucosa without causing necrosis or pigmentation of the tissue. The addition of procaine hydrochloride to the solution so that the final concentration was 0.25 per cent of procaine hydrochloride and 1 per cent of the gold compounds relieved the slight pain that accompanied the injection. A slight swelling following the injection was the only complication noted in any of the cases, and this was controlled by iced compresses or the application of an ice bag. The dosage of the intradermal injections used in our early cases varied from 10 to 25 mg. of gold compound per injection given once weekly. The results of the comparatively few injections given so far in the individual cases have been so gratifying that we are publishing this preliminary report that others may be given the chance to check and enlarge on this work. No untoward results with this method of treatment have been noted, and it is certain that should a patient have a severe reaction from an intradermal injection, an intravenous injection would assuredly produce a most unpleasant reaction. Lesions of the mucous membrane have responded in the same manner as the cutaneous lesions, the injections having been given into the submucosa.

The method presented in this paper is also being tried in suitable cases of lupus vulgaris, and the results of treatment obtained in that disease will be reported in full in a detailed paper on the entire subject.

2 East Fifty-Fourth Street.

114 East Fifty-Fourth Street

LEUKONYCHIA

ITS NORMAL OCCURRENCE AND CAUSATION *

PAUL L. SINGER

CHICAGO

Numerous reports have been presented in scientific periodicals on the occurrence of leukonychia, in which this condition has been treated mainly as a pathologic manifestation of some systemic disturbance. In this report I shall try to show: (1) that leukonychia occurs in a great percentage of all normal people, and (2) that a simple explanation can be formulated for its presence. If the fact is kept in mind that the finger-nail, phylogenetically, is in a disappearing, or at least a transitory, stage of evolution and at best is only a vestige, one can see that it is easily affected by changes in the condition of the body owing to its labile position. This is so well recognized that the nails are regarded as important diagnostic signs in dermatologic and systemic examinations.

Leukonychia has been observed as a concomitant phenomenon in various conditions. A few cases of congenital occurrence have been reported [1] in which both the finger-nails and the toe-nails were involved. Woolf [2] gave the impressive list of relapsing fever, typhoid fever, multiple peripheral neuritis, toxic gastro-enteritis, arsenic poisoning,[3] mental strain, frost-bite and trauma.[4] Menstruation also seems to affect its presence,[5] which, according to Becker, would show a hormonal influence; but this conclusion cannot safely be arrived at, as the increase in the metabolic rate that comes with the menstrual cycle will sufficiently explain its occurrence.

NORMAL OCCURRENCE

A group of one hundred normal persons was chosen at random for this part of the work; they were examined for traces of leukonychia. and classified according to the groups shown in the accompanying table.

* Submitted for publication, Dec. 30, 1930.

* From Loyola University School of Medicine.

1. Sibley, W. K.: Brit. J. Dermat. **23**:281, 1911.

2. Woolf, M. S.: Leukonychia Striata, Arch. Dermat. & Syph. **12**:520 (Oct.) 1925.

3. Hoffman, H.: Arch. f. Dermat. u. Syph. **153**:169, 1927. Weber, F. P.: Internat. Clin. **1**:108, 1918.

4. Netherton, E. W.: Leukonychia Striata, J. A. M. A. **93**:116 (July 13) 1929.

5. Becker, S. W.: Leukonychia Striata: Report of a Congenital Case, Arch. Dermat. & Syph. **21**:957 (June) 1930.

The results show a much higher percentage of occurrence normally than was anticipated or previously acknowledged. In all of these persons the leukonychia varied from small white spots to long stripes three fourths of the distance across the nail in length, which fall into Unna's classification as leukonychia punctata and leukonychia striata, respectively. No cases of total whiteness were seen in this group. Many persons who at the time of examination did not exhibit leukonychia informed the observer that at one time or another they had had white spots on their nails. If the examinations were repeated several times a year, the percentage would be raised still higher. Various causes, from "lie" spots to manicuring, were offered by the patients. The difficulty lies in the fact that as the nail grows but a thirty-second of an inch a week, several days must elapse before the white spot passes the lunula, which, itself being white, effectively conceals the supernatant white spot, and the patient forgets the orginal cause.

Incidence of Leukonychia Among One Hundred Normal Persons

Condition	Number of Cases	
	Men	Women
Number examined	76	24
On both hands	16	12
On left hand only	14	4
On right hand only	14	2
Total present	44	18
Wholly absent	32	6
Per cent present	58	75
Percentage of all cases present	62	

CAUSATION OF LEUKONYCHIA

In a review of the previous theories, the one concerning inclusions of air has so far found the greatest number of adherents. Heidingsfeld [6] and Becker [5] have shown, however, that in histologic sections no air spaces were seen, but only enlarged, acidophilic cells with large nuclei and keratohyaline granules. As an explanation of the presence of air in the sections of older accounts, it must be kept in mind that keratohyalin is much more soluble in strong acids than keratin, which is insoluble,[7] and as the technic requires softening of the nail in strong nitric acid, the keratohyalin can easily dissolve, leaving an air space between layers of insoluble keratin that would lead the observers to erroneous conclusions. Anatomically, the nail proliferates at the base of the nail root, where the only access to air would be through systemic

6. Heidingsfeld, M. L.: J. Cutan. Dis. **18**:490, 1900.

7. Bodansky, M.: Introduction to Physiological Chemistry, New York, John Wiley & Sons, 1927, p. 493.

channels, such as the blood stream or the lymph, and it is physiologically inconceivable that either of these should transport droplets of air.

Another theory of capillary damage and subsequent malnutrition [2] is not in line with the present views of keratinization.

All of the listed conditions in which leukonychia is found agree in one particular. Trauma, febrile attacks, the x-rays,[5] menstruation, hyperthyroidism and arsenic cause either a local or a general increase in the metabolic rate. Trauma causes it through local repair and vasodilatation. Menstruation, hyperthyroidism and febrile attacks cause it through systemic action; the x-rays and arsenic [8] are known to be markedly stimulating to the skin and its derivatives, and so cause an increase in the metabolic rate locally.

Keratinization is the process of the gradual fusion of the keratohyaline granules of the stratum germinativum with a gradual transformation into eleidin of the stratum lucidum and keratin of the stratum corneum, of the hair and of the substance of the nail.

Normally, the cause of keratinization is the gradual recession of the epithelial cells from the nutritive layer. As the cells recede they are less and less able to secure oxygen and food and are less able to remove waste products.[9] Keratinization is a protective response of the cells to the decrease in the metabolism of the cells. This is shown in tissue cultures, in which if the frequency of transplanting is diminished, the cells become keratinized. Likewise, most probably, in vitamin A deficiency the reduction in epithelial metabolism brings about a keratinization of all epithelia.

In leukonychia the white areas are characterized by the presence of keratohyaline granules in larger cells, which so diffuse the light as to prevent visibility of the pink vascular matrix below, causing the nail to appear white instead of pink.

As has been shown, in all cases of leukonychia there is an increase in the metabolic rate. This causes an increase in the permeability of the cells, and the cells as they are forced away from the root of the nail receive food and oxygen and remove their waste products for a longer time than normally. In this way keratinization is delayed, for the earlier condition of keratohyaline granules persists. But when the condition of increased metabolism ceases through removal of its cause, the permeability of the cells rapidly returns to normal. The outlying cells in the nail are suddenly deprived of food and so die before the keratohyaline granules can be transformed into keratin. There will,

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8. Osborne, E. D.: Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, Arch. Dermat. & Syph. **12**:773 (Dec.) 1925.

9. Cowdry, E. V.: Special Cytology, New York, Paul B. Hoeber, Inc., 1928, p. 33.

therefore, be dead cells present containing no keratin but only keratohyalin. As the nail grows, these islands are forced farther and farther out in the substance of the nail and so persist as the white spots, leukonychia, only to disappear when the nail is cut at the free edge.

In this light, the theory of damaged capillaries is a cause of leukonychia, not through lack of nutrition, which would merely cause an increased keratinization, but through an increase in the local metabolic rate in the repairing of the damage.

SUMMARY

1. Leukonychia was present in 62 per cent of a normal group of persons selected at random, and was more frequent in women than in men.

2. The theory of the inclusion of air is shown to be based on false interpretations of the observations.

3. As keratinization is due to decreased metabolism of the germinal layer, any increase in the metabolic rate will delay this, keratohyaline granules will persist, and leukonychia will result.

News and Comment

SECOND INTERNATIONAL CONGRESS FOR LIGHT

The secretary-general of the second International Congress for Light called attention, on June 4, to the fact that the congress is to be held in Copenhagen in 1932 and not in 1931. Detailed programs will be sent during the autumn of this year.

Abstracts from Current Literature

EDITED BY HERBERT RATTNER

CORRELATION OF THE ROENTGENOLOGIC PICTURE WITH THE GROSS AND THE MICROSCOPIC EXAMINATION OF PATHOLOGIC MATERIAL IN CONGENITAL OSSEOUS SYPHILIS. STAFFORD MCLEAN, Am. J. Dis. Child. **41**:607 (March) 1931.

This paper is based on the study of sixteen syphilitic infants varying in age from 1 to 13 months. Thirteen of the infants were under 3 months of age. Complete roentgenologic studies were made in all cases, and in each case there was roentgenographic evidence of pathologic changes in the bones. Autopsy was performed in all cases. The bones removed for histologic study were those that in the roentgenograms presented the most marked evidence of the disease. The cases studied ranged from those showing the earliest changes in the bone at the epiphyseal-diaphyseal junction to those with a most advanced type of osteochondritis showing extreme lawlessness of growth. The diaphyseal lesions ranged from slight changes in the cortices to well marked symmetrical osteomyelitic lesions involving large areas of the shaft. A number of the cases showed periosteal changes. Definite evidence of healing was shown in epiphyseal separations and in osteomyelitic lesions. All in all, the specimens consisted of nearly every variety of pathologic osseous change seen in congenital syphilis in the first few months of life.

The study of the roentgenograms in conjunction with the pathologic material has made quite clear and simple the explanation of osseous changes shown by the roentgenograms that formerly were obscure. The article is profusely illustrated with sixty-nine pictures, mostly photographs.

ANDERSON, Los Angeles.

GASTRIC SYPHILIS. PAUL A. O'LEARY, Am. J. Surg. **11**:286 (Feb.) 1931.

Of 151 patients with gastric lesions and syphilis, 89 were found to have gastric syphilis. The most practical method of arriving at a diagnosis is by the estimation of the response to antisyphilitic treatment in conjunction with a prolonged period of observation. These patients were treated with small doses of arsphenamine, mercury and bismuth. The criteria used in evaluating the therapeutic results were: rapid and persistent symptomatic relief from gastric symptoms, coincident with gain in weight and strength, decrease of anemia and increase in well-being, augmented by persistence of the improvement for at least two years. In one-half the cases, anatomic change in the gastric deformity may be expected. In the diagnosis, histopathologic studies, morphologic changes in the roentgenologic characteristics and restoration of gastric function must be considered. In the group studied, 73 per cent gave positive reactions to the Wassermann test of the blood as the only other evidence of syphilis, and in 6 per cent the reactions were negative. Various varieties of lesions are described, the differential diagnosis from other gastric lesions is considered, and the prognosis and treatment are discussed in full. The pertinent literature is critically reviewed.

RATTNER, Chicago.

ACROMEGALY WITH DIABETES MELLITUS AND XANTHOMA DIABETICORUM. ELAINE P. RALLI, Arch. Int. Med. **47**:329 (Feb.) 1931.

This article is the report of a case in which the symptoms of acromegaly had persisted since adolescence and had apparently preceded the diabetes. Typical small, pinkish-yellow tumors were present on the forearms and arms and around the knees. These disappeared under a diabetic diet, but soon recurred. A definite tumor of the pituitary gland, as well as severe diabetes mellitus, was found. Involution of the tumors was slow, though the hypercholesteremia and lipemia responded well to insulin and diet.

JAMIESON, Detroit.

On the Pathology and Pathogenesis of Scleroderma. Geoffrey Rake, Bull. Johns Hopkins Hosp. **48**:212 (April) 1931.

This article deals with a case of scleroderma associated with Raynaud's disease which was observed at intervals for about ten years. A roentgenogram of the sella turcica showed that it was greatly decreased in size. A complete examination, except of the brain, was made post mortem. The histologic changes in the left lower cervical sympathetic ganglion were interesting; it contained fewer ganglion cells than normal. Of the remaining ganglion cells, some were enlarged and pale and appeared "blown up." Others were small and shrunken. There were also atrophic changes in the voluntary muscles. Marked changes were present in the arteries with intimal proliferation. Dilatation of the esophagus and colon were present. No mention is made of any determinations for arsenic.

Anderson, Los Angeles.

Rupture of the Spleen in Malarial Therapy in Syphilis. S. H. Polayes and Max Lederer, J. A. M. A. **96**:1127 (April 4) 1931.

The authors abstract from the literature eight cases of rupture of the spleen following malarial therapy, and to these add a case that they have observed. The symptomatology is briefly described, and they stress the importance of its early recognition. They state that spontaneous rupture of the spleen occurs much more frequently in cases of malaria induced for neurosyphilis than in naturally acquired malaria. The increase in fibrous tissue in the capsule and septums with the resultant loss of elasticity that occurs in syphilis predisposes toward spontaneous rupture. The observations at autopsy are described in detail.

Erysipeloid in the United States. J. V. Klauder and Malcolm J. Harkins, J. A. M. A. **96**:1205 (April 11) 1931.

This is a full study of erysipeloid in the United States. Apparently this disease is more frequently obtained from contact with fish and *Crustacea* than from the flesh of swine, although the clinical picture is similar to the Germans' swine erysipelas in man. It is rare among veterinarians. It is more prevalent in hot weather and less common among the handlers of fish in the market, probably because the fish have been cleansed and packed in ice. It is an important occupational infection, because it is disabling and because treatment as a rule is inadequate. The clinical picture is described, and the various forms of treatment that have been recommended are evaluated.

Infantile Eczema with Especial Reference to the Use of a Milk-Free Diet. Lewis Webb Hill, J. A. M. A. **96**:1277 (April 18) 1931.

In cases of infantile eczema that are thought to be caused by milk, satisfactory results are obtained by the substitution of either evaporated milk or "Sobee." The latter is used in all cases in which there is a positive cutaneous reaction to milk protein or in very severe cases even if the cutaneous reaction is negative. The preparation Sobee is a light brown flour containing: soy bean flour, 67.5 per cent; barley flour, 9.5 per cent; olive oil, 19 per cent; sodium chloride, 1.3 per cent, and calcium carbonate, 2.7 per cent. The soy bean flour is rich in protein, and it contains the correct amino-acids for growth. The olive oil is a digestable fat, and the sodium chloride and calcium carbonate are added because soy bean flour is deficient in calcium, sodium and chlorine. It contains a sufficient amount of vitamin B, but not of the other vitamins, so that orange juice and cod liver oil must be given along with the Sobee. A full strength composition contains six level teaspoonfuls of the food to 7 ounces of water. It is adequate in basic composition and in caloric content; it is tolerated by the digestive tract, and it maintains nutrition. It is just another weapon in the attack on eczema, and the author emphatically states that he does not offer this as a

solution to the question of eczema. The article should be read for it is an excellent discussion of infantile eczema. External irritants and cutaneous tests are discussed adequately.

RINGWORM OF THE FEET. W. L. GOULD, J. A. M. A. **96**:1300 (April 18) 1931.

In a public high school it was found that about 50 per cent of the students were excluded from gymnastics because of tineal infection of the feet. Foot-baths containing a 15 per cent solution of sodium thiosulphate were installed between the locker-room and the shower-room. Each pupil on leaving the shower immersed the feet in this bath. In so doing, the solution was spattered over the floor of the locker-room so that the feet of the pupils were constantly in contact with the solution. A sulphate solution as low as 3 per cent was found efficient, so that by using a 15 per cent solution sufficient allowance is made for the dripping of plain water into the bath. The bath was changed frequently. In four weeks, with this procedure, the infection had practically disappeared from the school. In some cases, good results were obtained from the use of a 20 per cent powder of sodium thiosulphate in boric acid. This is dusted on the feet and in the footwear daily. The various clinical forms of tineal infection are well described.

RATTNER, Chicago.

FURTHER EXPERIENCES WITH NON-SPECIFIC LOCAL CUTANEOUS IMMUNITY TO STAPHYLOCOCCUS AUREUS: LOCAL NON-SPECIFIC PROTECTION. J. A. TOOMEY and S. O. FREEDLANDER, J. Exper. Med. **53**:363 (March) 1931.

Various kinds of local compresses were used on the abdominal wall of guinea-pigs: simple water, dry compresses, saline solution, mustard plasters, meat extract, peptone and normal horse serum. The first three mentioned were found to be slightly protective against massive inoculation with a culture of *Staphylococcus aureus*. Mustard plasters were not quite so effective as broth compresses; Liebig's meat extract was almost as good as the broth, and horse serum was quite as efficient. This protective action is nonspecific. If specific filtrates are applied at the time of inoculation or subsequent to it, no protection is conferred.

THE SKIN REACTIONS PRODUCED BY ALTERNATIONS OF HEAT AND X-RAY AT VARIOUS TIME INTERVALS. J. A. HAWKINS, J. Exper. Med. **53**:405 (March) 1931.

Suberythema doses of soft x-rays and heat of an intensity below the destructive point were employed. The results were the same whether x-rays or heat were applied first, and consisted of burns if the two applications were made within three hours of each other. With a longer interval, scaling was produced which was more pronounced and lasted longer than that produced by either heat or x-rays alone. Either type of radiation appears to be capable of sensitizing the skin to the action of the other.

JAMIESON, Detroit.

DERMATOSIS PAPULOSA NIGRA (CASTELLANI). F. A. DIASIO, M. J. & Rec. **133**:77 (Jan. 21) 1931.

Two cases of this condition are reported, both in young, full-blooded Negresses. The histopathologic picture in one case supported the view that dermatosis papulosa nigra is an ectodermal nevus.

THE ROLE OF HEREDITY IN PSORIASIS. HENRY D. NILES, M. J. & Rec. **133**:80 (Jan. 21) 1931.

A study of 375 case records indicates that psoriasis is not a hereditary disease in the ordinary sense of the term, but that its incidence is higher in families in

which psoriasis was present. Familial incidence was found to be 24 per cent, and in 13 per cent of the patients, a parent, grandparent or child was afflicted.

RATTNER, Chicago.

A COMPARISON OF THE ROENTGEN RAY WITH OTHER FORMS OF RADIANT THERAPY IN TREATING SKIN DISEASES. HERBERT H. BAUCKUS, New York State J. Med. **31**:345 (March 15) 1931.

The studies are based on the observation of more than 5,000 cases during the past four years. A combination of x-rays and radium with ultraviolet light and other local applications was found to be more successful than the use of either agent alone; in fact, ultraviolet light alone was not considered to be much of a therapeutic aid. X-rays and radium were used interchangeably except when one or the other was more convenient of application owing to the location or size of the lesion. Radium proved superior in the treatment for angioma, keloids, lupus erythematosus, lupus vulgaris and roentgen keratoses. In all other conditions roentgen treatment was given the preference because the author felt that he could control the practical dosage of x-rays better than that of radium. The mercury arc in quartz was considered to be the only reliable source of ultraviolet ray radiation, and a warning was issued to beware of the many substitutes.

BACTERIOPHAGE: ITS APPLICATION IN DERMATOLOGICAL PRACTICE. ANTHONY C. CIPOLLARO, New York State J. Med. **31**:349 (March 15) 1931.

The principles, methods of preparation and properties of bacteriophage are discussed in some detail. Its greatest field of usefulness in dermatology seems to be in cases of sycosis vulgaris, staphylococcic abscesses, staphylococcic infected cysts, carbunculosis, furunculosis, acne vulgaris (pustular type), chronic staphylococcic pyoderma and impetigo contagiosa. The bacteriophage may be either applied locally to the surface of the lesion, injected in or about the area of disease or given subcutaneously at some distant site, apparently with the same effect. Before the bacteriophage is used, a culture from the pus of the lesion should be made and the organisms should then be tested for susceptibility to that particular bacteriophage. If the bacteriophage is potent, and if it has the ability to lyse the organism, a favorable result with this treatment may be predicted. Reactions following the administration of bacteriophage are few and are of little consequence.

TRAUB, New York.

SKIN-DISEASES DUE TO MONILIA AND OTHER YEAST-LIKE FUNGI. J. M. H. MACLEOD, Brit. J. Dermat. **42**:549 (Dec.) 1930.

The fungi and the cutaneous lesions associated with their presence are described. Although the name "yeastlike fungi" includes *Monilia, Pityrosporon, Blastomyces* and *Coccidioides*, MacLeod has confined his paper to *Monilia* and *Pityrosporon*, which are pathogenic fungi, in contradistinction to *Saccharomyces*, which is nonpathogenic and when present in the skin leads a harmless saprophytic existence. The lesions of cutaneous moniliasis are discussed under two headings: (*a*) widely disseminated or (*b*) strictly localized; photographs are shown illustrating the fungi and the variety of clinical pictures produced. *Pitryrosporon* or the "spore of Malassez" is discussed, and its differentiation from *Monilia* on the basis of morphology and cultural characteristics is brought out.

THE PATHOGENICITY OF MONILIA AND OTHER YEAST-LIKE FUNGI. G. B. DOWLING, Brit. J. Dermat. **42**:562 (Dec.) 1930.

The pathogenicity of various species of *Monilia* is discussed on the basis of two types of tests. From the results of experiments on human subjects Dowling feels that certain guarded conclusions can be drawn: 1. The three varieties of *Monilia* experimented with are at times parasitic on human skin. The experiments of

Greenbaum and Klauder, who cultivated fungi, probably of this group, from a large number of normal subjects, suggests also that they may be normally saprophytic. 2. Their pathogenicity is of a low grade order, the degree of reaction being dependent as much on the soil as on inherent virulence. 3. They may acquire increased virulence in the parasitic phase. This is shown by the positive results of experimental transplantation of fungi freshly grown from lesions. A discussion of experimental studies made on laboratory animals with various species of *Monilia* is presented, with references to the literature.

SOME REMARKS ON INFECTIONS OF THE SKIN BY MONILIA AND OTHER YEAST-LIKE ORGANISMS. B. BLOCH, Brit. J. Dermat. **42**:569 (Dec.) 1930.

Bloch discusses the following forms of *Monilia* infection that he has encountered in his material: (*a*) erosio interdigitalis blastomycetica, viz., oidiomycetica; (*b*) the pustular oidiomycoses; (*c*) oidiomycoses occurring with diabetes, and (*d*) onychomycosis oidiomycetica (oidiomycosis of the nails). From his personal experience, he feels that under especially favorable external conditions, among which moistening of the skin, warmth and also a lowered vital resistance of the skin (e. g., in diabetes) play an essential rôle, *Oidium* is able to produce pathogenic effects in the human skin, i. e., to call forth various dermatoses which are, on the whole, characterized by a harmless course.

A new phase of the problem of dermatoses due to fungi is characterized by the fact that conditions that had hitherto been regarded as belonging to the eczemas are now considered to be oidiomycoses. According to the modern, i. e., allergic, conception of eczema, special importance is attached not only to the direct infection of the skin by fungi, but also to the remote lesions caused by hypersensitivity to the fungi. Thus, conceptions like "levurides," "oidiomycides," etc., have been formed. Bloch states that the research work on the group of dermatoses caused by the fungi mentioned is rendered difficult by two factors, and that a real step forward can hardly be realized before these difficulties are removed: (1) the great uncertainty as to the botanic classification and nomenclature of these fungi, and (2) the fact that the fungi referred to can also occur as saprophytes on the skin of normal persons.

SKIN TEMPERATURE IN ALOPECIA AREATA. A. C. ROXBURGH, Brit. J. Dermat. **43**:20 (Jan.) 1931.

The results of observations on the temperature of the skin in a group of cases of alopecia areata are presented. By means of a sensitive thermocouple, illustrated diagrammatically, the temperature of patches of alopecia areata and of the adjoining normal skin was recorded. The observations are presented in three tables and are discussed by Roxburgh. He concludes with the following summary: Experiments with a sensitive thermocouple on twenty-six patches of alopecia areata showed that there was no substantial or essential difference in surface temperature between areas of alopecia areata and the adjoining normal skin. This seems to show that alopecia areata is not due to restriction of the blood supply to the affected area as has been suggested by some authors. Evidence is brought forward that the erythema following a dose of ultraviolet light only increases the surface temperature by about 0.5 C., so small a rise being inconsistent with any appreciable dilatation of the deeper arterioles. It is therefore suggested that the beneficial results of ultraviolet light in this disease do not depend on its vasodilator effect, but on its stimulating effect on cell division and keratinization in the epidermis, of which the cells of the hair matrix are developmentally a part.

WIEN, Chicago.

CUTANEOUS HORN ON AN AMPUTATION STUMP. F. E. MAYNE and LAURENCE O'SHAUGHNESSY, Brit. M. J. **1**:624 (April 11) 1931.

A cutaneous horn appeared on the end-scar of a stump fifty years after amputation. There was no evidence of epithelioma. A large painful neurofibroma was found in the base of the scar.

BLACK HAIRY TONGUE. HUMPHREY H. GLEAVE and SAMUEL HALLAM, Brit. M. J. **1**:663 (April 18) 1931.

In the case reported, the condition disappeared readily after the use of a mouth wash of potassium and phenol. A *Cryptococcus* was isolated from the lesion. The authors suggest that this *Cryptococcus* may be a *Saccharomyces* which, owing to a long stay in the mouth, has become asporogenic.

A CASE OF BLACK TONGUE. H. MORTIMER WHARRY, Brit. M. J. **1**:664 (April 18) 1931.

The author concludes from a study of his case that: 1. Black tongue may spread over the posterior third of the tongue, and is not confined to localized patches anterior to the circumvallate papillae. 2. The dark color is caused by the fungus and not necessarily by any changes in the papillae of the tongue itself. 3. The disease may be of long standing and yet not cause hypertrophy of the papillae. 4. Hypertrophy of the filiform papillae is probably due to continuous irritation of the tongue at one particular spot where the fungus has taken a firm hold. 5. The growth of the fungus is the primary condition, and may exist without lingual hypertrophy.

UNUSUAL DISTRIBUTION AND MORPHOLOGICAL MODIFICATION OF COMEDO. J. GOODWIN TOMKINSON, Brit. M. J. **1**:666 (April 18) 1931.

A patient was observed in whom comedones roughly simulating patches of xanthoma palpebrarum in distribution and color appeared on the eyelids. There were yellowish, raised, circular plaques with central black spots. The author has never before observed comedones on the upper lids. The patient worked with oils, and perspired freely; blackheads formed frequently around the lower eyelids. It was thought that the unusual outlines were due to the underlying dense fibrous tissue of the tarsal plates and the diurnal palpebral movements.

LEPROSY. E. H. MOLESWORTH, M. J. Australia **1**:324 (March 14) 1931.

This is a brief but excellent summary of the subject of leprosy. The article was written by invitation, and the subject is treated as in a textbook, with especial emphasis on diagnosis. Treatment is not considered.

RATTNER, Chicago.

ERYTHEMA ELEVATUM DIUTINUM. ALICE CARLETON, Proc. Roy. Soc. Med. **24**: 392 (Feb.) 1931.

In a man, aged 38, a nodule developed on the left arm in October, 1929. When seen in November, he showed a raised vivid erythematous ring of rubber-like consistency surrounding a flat, slightly pigmented center. Its dimensions were then 4 by 5 inches (10.1 by 12.7 cm.). The epidermis was movable, though not freely, over the induration which itself was easily movable on the deeper tissues. The ring appeared to widen and break up into scattered nodules. Some of these disappeared, but some were still present. In February, June and August of the following year, lesions appeared on the right side of the chest, the back of the neck and the interscapular region. Their appearance and evolution were similar except that on the chest the original nodule tended to break up into smaller nodules without any definite ring formation. The lesion on the neck had nearly disappeared. The first sign of a developing lesion was a rather diffuse hardening, which gradually became more salient and circumscribed. No lesion resembled the pearly nodule of granuloma annulare. After eight injections of a sensitized streptococcal vaccine all the lesions had completely disappeared.

PARONYCHIA DUE TO A YEAST-LIKE ORGANISM WITH CURIOUS DISCOLORATION OF THE NAILS. A. M. H. GRAY, Proc. Roy. Soc. Med. **24**:397 (Feb.) 1931.

In a housewife, aged 36, inflammation had begun at the side of the left thumb-nail about one year before. There was no discharge from beneath the nail-fold at this time. Three months before this report a similar condition developed around the nail of the left index finger. Since the onset an occasional bead of pus had been squeezed from the nail-folds. The nails of the thumb and index finger of the left hand were of a mahogany color on all parts not covered by the nail-fold; below this the nails were normal in color. The color was easily removed by scraping. The nail-fold of the left thumb was swollen all around and tender; that of the left index finger was swollen on the radial side and also tender. No pus was present beneath either fold. The nail showed irregular transverse grooving. The index finger-nail showed slight separation from the bed on the radial side near the free end. A yeastlike organism was recovered from both nail-folds.

GUY, Pittsburgh.

INFLUENCE OF THE AMOUNT OF BLOOD CHOLESTEROL ON THE SEROLOGIC REACTIONS FOR SYPHILIS (WASSERMANN, HECHT, DESMOULIERES). R. J. WEISSENBACH and J. MARTINEAU, Bull. Soc. franç. de dermat. et syph. **38**: 150 (Feb.) 1931.

At a recent meeting, Gougerot and Rabu reported the apparent association of hypercholesteremia and Wassermann-fast syphilis. In view of this, Weissenbach and Martineau report forty-eight cases of syphilis in which estimations of the blood cholesterol and several Wassermann tests were made simultaneouly for the purpose of determining if the cholesterol content had any influence on the serologic result. The results do not allow the deduction that hypercholesteremia is a direct or unique cause of the persistence of a positive seroreaction when an increased cholesterol content of the blood is present. It may be a simple coincidence, or the two disorders may be dependent on the same cause (syphilis). The syphilitic infection may act by two different mechanisms producing a serologic change, on the one hand, and a disturbance of the lipid metabolism, on the other. In this eventuality, it is comprehensible that treatment directed to the syphilis and the underlying factors in the lipid disturbance may occasion a decrease in blood cholesterol and a negative seroreaction. This result, however, does not permit the conclusion that the negativity of the Wassermann test is a direct consequence of the lowered blood cholesterol, since one may obtain the latter without modification of the former.

GOUGEROT AND RAGU'S REPORT ON THE RELATION OF THE CHOLESTEROL OF THE BLOOD TO WASSERMANN-FASTNESS. E. SCHULMANN and G. LÉVY, Bull. Soc. franç. de dermat. et syph. **38**:155 (Feb.) 1931.

The authors refer to several earlier reports on the relation between the cholesterol content of the blood and Wassermann-fast cases. In eighteen patients with an increased cholesterol content they found two with positive Wassermann reactions; both had syphilis. In two late cases of syphilis with partially positive reactions they tried to activate the serologic test by increasing the blood cholesterol, but both attempts were failures. Experiments along the same line on animals was likewise fruitless. The authors are therefore unable to corroborate Gougerot and Ragu's observations.

ERYTHRODERMA DUE TO GOLD THERAPY. LORTAT-JACOB and JAIME, Bull. Soc. franç. de dermat. et syph. **38**:169 (Feb.) 1931.

A patient with pulmonary tuberculosis had been treated with a gold compound for about a year. Erythroderma developed one month after the last injection. It was preceded by an intense pruritus. The condition cleared up in about a week.

DILUTED GLYCERIN AS AN AGENT IN THE OCCLUSION OF VARICOSE VEINS. H. JAUSION, E. CARROT and A. GERVAIS, Bull. Soc. franç. de dermat. et syph. **38**:171 (Feb.) 1931.

The authors have found the following solution useful in the treatment for varicose veins by injection.

	Cc.
Glycerin	126.0
Distilled water	200.0

Phenolate fuchsin (Ziehl) 1 drop to each cubic centimeter for sterilization, or heat to 100 C. for thirty minutes.

This solution produces very little discomfort if, by mischance, some of it is injected outside the vein. It is well tolerated. The authors have employed it in about 300 cases.

PRIMARY RETRO-AURICULAR INTERTRIGO DUE TO YEASTS: SECONDARY ECZEMA OF THE ARMS AND LEGS; BIOLOGIC REACTIONS. P. RAVAUT and LONGHIN, Bull. Soc. franç. de dermat. et syph. **38**:177 (Feb.) 1931.

Ravaut and Longhin report a case of bilateral retro-auricular exudative dermatitis with many scattered scaly patches on the extremities. In the aural lesions they found streptococci, staphylococci and *Cryptococcus*. Intradermal reactions were positive only to the latter. The authors believe that the outcome of such biologic reactions determines the pathogen in each case. Further, the scaly lesions are secondary and allergic, since they disappear when the primary focus is eradicated and they are activated when the specific antigen is injected.

UNGUAL MYCOSIS. MILIAN and PAPADOPOULOS, Bull. Soc. franç. de dermat. et syph. **38**:181 (Feb.) 1931.

A patient showed a slight paronychia with dystrophy of the nail plate. From the nail *Penicillium brevicaule* was cultured. In the discussion Sabouraud said that his investigations seemed conclusive that *Trichophyton* alone is pathogenic in mycosis of the nails.

TUBERCULOSIS OF THE HYPODERM SIMULATING MADURA FOOT. MILIAN and R. DEGOS, Bull. Soc. franç. de dermat. et syph. **38**:186 (Feb.) 1931.

Milian and Degos saw a patient whose left foot was markedly enlarged, with a voluminous tumefaction extending from the internal malleolus over the dorsum. The aspect suggested Madura mycosis. Laboratory examinations repeated over a considerable period showed no fungi. Finally, after a section had shown a picture suggesting tuberculosis, inoculation of guinea-pigs demonstrated that infection.

DERMATITIS MEDICAMENTOSA FROM CARBROMAL. GOUGEROT and J. MEYER, Bull. Soc. franç. de dermat. et syph. **38**:206 (Feb.) 1931.

A patient had an extensive eruption composed of purpuric spots, brown macules and eczematized patches. The authors believe that it is the first recorded case of an eruption caused by carbromal.

IDIOPHAGEDENA OF THE VULVA: GEOMETRIC PHAGEDENA OF BROCQ AND SIMON. P. CHEVALIER, LÉVY-BRUHL and MORICARD, Bull. Soc. franç. de dermat. et syph. **38**:212 (Feb.) 1931.

The authors report a case of extensive and rapid ulceration of the vulva of a phagedenic type from which they isolated an exceptionally virulent staphylococcus. Autovaccine therapy produced rapid healing.

GOLD THERAPY WITH SEVERE SHOCK. HISSARD, Bull. Soc. franç. de dermat. et syph. **38**:224 (Feb.) 1931.

Hissard has found only a few reports of severe shock from injections of a gold preparation. He reports a case of lupus erythematosus in which mild shock developed during the first injection. Repetition of the symptoms occurred after the following two doses.

THE WEIL-KAFKA HEMOLYSIN REACTION IN THE STUDY OF MENINGEAL PERMEABILITY. R. DEMANCHE and L. VAN HUÉ, Bull. Soc. franç. de dermat. et syph. **38**:235 (Feb.) 1931.

The authors employed a simplified technic of the Weil-Kafka method for the detection of antisheep hemolysin in the spinal fluid. They found the reaction negative in all diseases, including syphilis, in which the central nervous system was not involved. However, it was constantly positive in dementia paralytica and rapidly regressed under the influence of malaria and drug therapy for that disease. It furnishes a means of estimating the functional state of the choroid plexus and, in dementia paralytica, an index of the effect of treatment.

GOLD THERAPY IN SYPHILIS. F. LEBEUF and H. MOLLARD, Bull. Soc. franç. de dermat. et syph. **38**:251 (Feb.) 1931.

Lebeuf and Mollard report a modest number of cases of syphilis in which gold preparations were given. Injections of a preparation containing the disodium derivative of 4-amino-methylsulphuric acid-2-auromercaptobenzene-1-sulphonic acid were found painful, but this drug in intramuscular injections seemed more effective than gold sodium thiosulphate given intravenously. The use of gold in syphilis is in its infancy and requires further study; it may prove of value in Wassermann-fast, nervous and arsenic-resistant patients.

KERATOTIC CAVERNOUS NEVI OF THE SCROTUM. P. VIGNE, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Lyon) **38**:261 (Feb.) 1931.

A patient presented a number of isolated lesions on the scrotum. They ranged from small, ruby red papules to larger, violaceous, pedunculated and verrucous elements. The patient was 43 years of age, and the lesions had first developed in 1929. Histologic study of the smaller lesions showed a collection of thin-walled vascular spaces in the upper cutis, while the larger lesions revealed hyperkeratosis and the structure of a cavernous angioma. Vigne discusses the differential diagnosis from angiokeratoma of Mibelli. His cases seem similar to those reported in this country by Fordyce and Sutton. The lesions appear to be nevi of tardy development.

MICHAEL, Houston, Texas.

GENERAL RULES IN ANTISYPHILITIC TREATMENT: THE DOCTRINE OF INDEFINITE PERIODICAL SURVEILLANCE AND THE NECESSITY OF "CONSOLIDATION" TREATMENT DURING MANY YEARS. GOUGEROT, Hyg. soc., Jan. 10, 1931, p. 783.

Gougerot believes with the majority of French syphilologists that there are no absolute criteria for the cure of syphilis. Therefore, fearing unexpected relapses, he requests an almost lifelong treatment. He divides it into three periods. The first he calls the treatment of "attack," the second period, the treatment of "consolidation," and the third, the "assurance" treatment. The "attack" treatment lasts about one year, and consists of five or six courses of arsphenamine, mercury and bismuth (first course, arsphenamine with or without bismuth; second course, arsphenamine with or without mercury; third course, bismuth; fourth

course, bismuth; fifth course, arsphenamine). Gougerot insists on as early treatment as possible, with the maximal doses that can be tolerated by the patient, whether the infection is recent or old, and even if there is only a positive Wassermann reaction and no other signs; also whether the condition is benign or malignant, as a seeming benign condition may later attack vital viscera. The intervals between courses should not be shorter or longer than from three to four weeks. Besides the classic Wassermann test, Gougerot suggests a Wassermann-Hecht and a Wassermann-Desmouliere. Fever or malarial treatment is to be used only in cases that are resistant to other therapy.

He calls the second period the "consolidation" treatment, because it consolidates the results of the "attack" treatment. It lasts two years if the "attack treatment" has started in the first two weeks after the appearance of the chancre and four years if the Wassermann reaction was positive when the "attack treatment" was begun. In spring (March or April) and fall (September or October) he gives a course of bismuth; in winter (January) and summer (July), a course of mercury. This period of treatment should prevent ocular and meningeal involvement, which is seen in patients not receiving this consolidation treatment. After this period the author advises the reactivation Wassermann test according to Milian: no treatment for from five to six months, then three injections of arsphenamine and from fifteen to twenty days later a Wassermann-Desmouliere test. If a lumbar puncture was not performed at the end of the first period, it should be requested at the end of this period.

Gourgerot calls the third period the "assurance treatment," as it gives assurance against any relapse. It consists in the following treatment: from the third to the fifth year, in spring and autumn, a course of bismuth, in January and July, six injections of mercury (thirty-six injections in all during a year). From the eleventh to the twentieth year, four courses of treatment a year. The mercury may be administered by mouth. From the twenty-first to the twenty-fifth year, two courses in a year: bismuth in spring and mercury in autumn.

In favor of this third period, the author mentions the famous statistics of Fournier; namely, that 87 per cent of dementia paralytica occurs from the sixth to the fifteenth year after infection.

BLOOM, New York.

THE PRESENCE OF SPIROCHETES IN THE SPINAL FLUID IN EARLY SYPHILIS. R. GEIGER, Arch. f. Dermat. u. Syph. **162**:473 (Jan. 24) 1931.

In a group of thirty patients nearly all of whom had early syphilis, spirochetes were found in the spinal fluid in twelve. Of these twelve patients, two had chancres and showed a positive reaction to the Wassermann test of the blood, eight had secondary syphilis; one, active tertiary syphilis, and one, latent syphilis. Only five showed a positive reaction to the Wassermann test of the spinal fluid, namely, four of the patients with secondary syphilis and the one with latent syphilis. Spirochetes were observed in spinal fluids negative to all tests used at the present time and could be found prior to the outbreak of a generalized exanthem.

CLINICAL, EXPERIMENTAL AND CHEMICAL STUDIES ON THE INFLUENCE OF DIET ON INFLAMMATORY CHANGES IN HEALTHY AND DISEASED SKIN. J. DÖRFFEL, Arch. f. Dermat. u. Syph. **162**:621 (Jan. 24) 1931.

The healing effect of a salt-free diet (modification of Hermannsdorfer) in lupus vulgaris is confirmed. Histologic studies show that the cells of the vessel walls play a preponderant part in the process of healing. Several cases of eczema, psoriasis and pemphigus were improved by the same diet.

The inflammatory response of the skin was increased during the treatment and returned to normal when the usual diet was resumed.

The Hermannsdorfer diet is slightly acidic and produces a moderate dehydration of the entire body, especially of the diseased areas.

ANIMAL EXPERIMENTS REGARDING THE INFECTIOUS-TOXIC ORIGIN OF PEMPHIGUS VULGARIS AND DERMATITIS HERPETIFORMIS. E. URBACH and F. REISS, Arch. f. Dermat. u. Syph. **162**:713 (Jan. 24) 1931.

Paralysis of the posterior extremities, followed by death, was produced in some rabbits by the injection of blood and the contents of bullae from patients with pemphigus vulgaris and dermatitis herpetiformis into the veins, cisternal areas and skin of the ear; in other rabbits, the injection produced a similar paralysis with recovery, and in some, no effect was noted. Histologically, infiltrations of the meninges, inflammatory lesions and hemorrhages in the spinal cord and in various portions of the brain were noted. The authors consider that their observations tend to support the theory that the origin of these diseases is due to an infectious toxin.

LOCALIZED HYPERTROPHY OF THE HAIRS AFTER EPILATION OF THE SCALP WITH THE X-RAYS. A. DOSTROWSKY, Arch. f. Dermat. u. Syph. **162**:739 (Jan. 24) 1931.

In thirty-eight cases of tinea of the scalp, a localized hypertrophy of the hairs was observed during the period of regeneration after epilation by x-ray. This condition was shown by longer, thicker, more deeply pigmented and more closely set hairs. In most of these cases, the area affected was one that had been the seat of an irritative process, such as a pustular inflammatory reaction or prolonged irritative local treatment either before or after the roentgen treatment.

MONASH, New York.

THE TENDENCY TOWARD THE FORMATION OF KELOIDS IN ARTHRITIS DEFORMANS. EMANUEL WOHLSTEIN and LUDWIG TORMA, Dermat. Wchnschr. **92**:385 (March 14) 1931.

Five cases are reviewed in which keloids developed in patients with arthritis deformans; some were apparently spontaneous and the others the result of ordinarily insignificant trauma. The authors consider that the same mesodermal deficiency predisposes to both conditions.

SALT OF AURO-ALLYLTHIOCARBAMIDOBENZOIC ACID IN THE TREATMENT FOR LUPUS ERYTHEMATOSUS. JOSEF KONRAD, Dermat. Wchnschr. **92**:391 (March 14) 1931.

The author has treated fifty patients for lupus erythematosus with a complex salt of auro-allylthiocarbamidobenzoic acid containing 43 per cent of gold. In two instances a severe generalized toxic dermatitis occurred, in the one, after the administration of a total of 3.93 Gm. and in the other, after only 0.65 Gm. had been injected.

It is advisable to start treatment for lupus erythematosus with this gold salt after the acute inflammatory stage has passed. The first dose should be 0.01 Gm., increased at intervals to a maximum of 0.5 or in rare instances, 0.75 Gm. The higher doses should be given at intervals of from ten to fourteen days, and the treatment should be interrupted if there is a local reaction or if there are headaches, pains in the joints, itching, etc. The urine was examined frequently, though pathologic conditions did not occur in any of the fifty patients treated, including the two in whom dermatitis developed. The treatment has failed to improve or cure less than 20 per cent of the patients, and the drug is considered less toxic and therapeutically more active than other gold compounds.

THE RARER FORMS OF LICHEN RUBER. WILHELM RICHTER, Dermat. Wchnschr. **92**:413 (March 21) 1931.

A case is reported in which the eruption is diagnosed as a condition resembling both lichen albus and lichen sclerosus, being similar to each in certain respects. The author concludes that it is possible that the difference between these two forms consists merely in a different stage of the same condition.

TREATMENT FOR LUPUS VULGARIS WITH ROENTGEN RAYS. CARL STERN, Dermat. Wchnschr. **92**:418 (March 21); 456 (March 28) 1931.

The author reviews the history of the use of the x-rays in the treatment for lupus vulgaris. As a result of histologic and clinical observations, he concludes that: 1. Roentgen rays have the property of stimulating the development of connective tissue in lesions due to lupus. 2. The rays destroy the lymphocytes, freeing substances that act as a stimulant to the proliferation of surrounding tissue. 3. The intima cells of the capillaries are stimulated to the development of epithelial cells. 4. Some of the newly formed epithelioid cells are destroyed, and some become connective tissue cells.

The beneficial effect on the lesions in lupus is obtained only when the dosage is correct, from 5 to 8 Holzknecht units with from 1 to 3 mm. of aluminum filtration. Other methods of treatment, especially generalized radiation with ultraviolet light, should be used with roentgen therapy.

SYPHILITIC FEVER. LADISLAUS STRAUSZ, Dermat. Wchnschr. **92**:425 (March 21) 1931.

The literature considering the occurrence of fever in syphilis is reviewed. A report of a case is given in a man, aged 34, who had a temperature of from 38 to 39 C. (100.4 to 102.2 F.) for two months. The physical examination showed a systolic murmur at the apex, an accentuated second aortic sound and a markedly enlarged spleen. The white blood cells numbered 3,600, and the Wassermann reaction was negative. The condition gradually cleared up under therapy with neoarsphenamine.

ORIGIN OF THE PORTWINE STAINS ON THE NAPE. RUDOLPH BEZECNY, Dermat. Wchnschr. **92**:453 (March 28) 1931.

The occurrence of red spots of varying intensity (Nackenflecks) on the nape is common, being noticeable less frequently in men than in women. From a study of a fetus 30 cm. long, presenting one of these vascular dilatations, the author concludes that the spots are due to stretching of the skin during fetal life.

A CASE OF VARUS NODULOSUS OF BROOKE. FRANZ VON VERESS, Dermat. Wchnschr. **92**:481 (April 4) 1931.

The author recalls the description of the condition named varus nodulosus by Brooke in 1906. He reports a case that was practically identical, and concludes that it belongs with the papulonecrotic tuberculids on the basis of the histologic observations as well as the clinical course.

VITAMIN FEEDING IN STAPHYLOCOCCIC INFECTIONS OF THE SKIN. MARTIN SCHUBERT, Dermat. Wchnschr. **92**:486 (April 4) 1931.

Four groups of five guinea-pigs were given, respectively, vitamin B, vitamin D, calcium and a homeopathic preparation of sulphur with their regular food. A fifth group was used as a control. On the fifteenth day all were given an intracutaneous injection of a culture of staphylococci. No marked differences in susceptibility were noted. In another experiment the groups of animals were fed with varying combinations of vitamins and calcium and sulphur, again with no notable differences in the result. A diet rich in vitamins was prescribed for a group of clinical patients with pyogenic infections of the skin, but there was no apparent benefit.

FEEDING OF VITAMIN IN STAPHYLOCOCCIC INFECTIONS OF THE SKIN. W. PFANNENSTIEL, Dermat. Wchnschr. **92**:489 (April 4) 1931.

The author, with Scharlau, has previously reported the effect of the feeding of vitamins in protecting experimental animals against staphylococcic infections.

He criticizes Schubert's experiments on the basis that the dosage was insufficient and on account of the inaccuracy of the method of mixing the therapeutic substance with the food.

THE SIMPLIFICATION OF GRENZ RAY THERAPY BY MEANS OF A NEW HALF VALUE METER. HEINZ BERGER, Dermat. Wchnschr. **92**:492 (April 4) 1931.

An instrument is described by which the thickness of aluminum necessary to absorb 50 per cent of the oversoft roentgen rays may be calculated in thousandths of a millimeter.

THE MINERAL CONTENT OF THE SKIN UNDER NORMAL AND PATHOLOGIC CONDITIONS: VI. VARIATIONS IN THE POTASSIUM, CALCIUM, CHLORIDE AND WATER CONTENT OF THE SKIN OF RABBITS AND GUINEA-PIGS UNDER PROPORTIONATE NOURISHMENT AND IN STARVATION AND THIRST. E. NATHAN and F. STERN, Dermat. Ztschr. **60**:299 (March) 1931.

The authors studied the variation in mineral content of the skin of rabbits and guinea-pigs kept as nearly as possible under comparable conditions of life and diet. They made use of their own microchemical method, which permitted the determinations to be made with small pieces of the skin of the same animal at various intervals. The apparently normal variation was marked, especially in the case of the rabbits.

The same experiment was carried out with starving and with starving and thirsting animals. In general, demineralization and dehydration were demonstrated, but in a few instances there was little or no change, which may be explained by the mutual relation between the skin and other water and mineral depots of the body, such as the connective tissue, muscles and joints.

THE OCCURRENCE OF APOCRINE GLANDS. K. H. VOHWINKEL, Dermat. Ztschr. **60**:314 (March) 1931.

The author agrees with certain other investigators in the contention that the presence of apocrine glands in the axilla may be etiologically important in the production of Fox-Fordyce disease, owing to an alteration in the character of the sweat excreted. A case of myxohidradenoma neviforme was studied in which some of the glandular structures were pathologically similar to apocrine glands, except that the ducts as shown in serial sections did not open through the follicles.

ETIOLOGY OF TRICHOTILLOMANIA. ARTHUR SCHWARZKOPF, Dermat. Ztschr. **60**:321 (March) 1931.

Four patients with trichotillomania are described, the youngest less than 1 year of age and the oldest, 22. In no case was there a dermatologic condition to cause pruritus. The literature is reviewed briefly, and the author concludes that it is necessary to analyze each individual case to determine the appropriate psychic therapy. Mechanical methods are considered useless.

TAUSSIG, San Francisco.

TWO EXTRAGENITAL HYPERTROPHIC CHANCRES. OLGA VALENTOVA, Česká dermat. **11**:243 (Dec.) 1930.

This is a report of two extragenital hypertrophic chancres of unknown, probably accidental, indirect mode of infection (Fournier's "infection médiate"). One was located on the cheek and the other (duplex) on the nose.

EXPERIMENTAL SYPHILIS IN RABBITS. K. PERNER and J. UNGAR, Česká dermat. **12**:1 (Jan.) 1931.

For inoculation, the authors used human syphilitic material from fourteen patients with chancres; four of the patients had condylomas (solid material); in

six instances the material was taken from vesicles produced by cantharides on macular exanthems and in two cases from blood in the secondary stage. In eight cases the organs of animals were used. Of fifty-two rabbits, eleven showed macroscopic manifestations of syphilis verified also microscopically. Lesions produced by testicular inoculation showed chancre in two instances, erosion in one and localized or diffuse orchitis in seven. Ocular inoculation produced keratitis in three cases.

THERAPY FOR DEEP TRICHOPHYTOSIS. M. BEZECNA, Česká dermat. **12**:6 (Jan.) 1931.

A solution of ferric chloride (equal parts of crystals of ferric chloride and water) was used in stubborn cases of trichophytosis profunda barbae with prompt results. After epilation and removal of crusts, the solution was painted on the lesions once a day.

THE OXYACETYLAMINOPHENYLARSENATE SALT OF DIETHYLAMINE IN HOSPITAL AND AMBULATORY PRACTICE. O. ZBORILEK, Česká dermat. **12**:9 (Jan.) 1931.

The author employed the oxyacetylaminophenylarsenate salt of diethylamine in 195 cases of syphilis. He recommends it particularly in neofast and neointolerant cases. Given intravenously, it causes fever in some cases. Given subcutaneously, it often leaves painful indurations. Intramuscular injections, however, are well tolerated. The author never gives more than 3 cc. three times a week. The advantages of acetylarsan are that it is a good antisyphilitic preparation suitable for ambulatory cases, and that is is painless, easily administered and of low toxicity; the shortened course of treatments (three and one-half weeks) is comparatively inexpensive. The author recommends its trial in resistant psoriasis and chronic eczema.

SPINKA, Texarkana.

ENDOCRINE ANOMALIES IN RECKLINGHAUSEN'S DISEASE. B. A. RUSSAKOW, Sovetski Vestnik Dermat. **9**:2 (Jan.) 1931.

The author reports a case of Recklinghausen's disease in a woman aged 22, who showed also disturbances of several endocrine glands: parenchymatous hyperplasia of the anterior lobe of the hypophysis, hyperpituitarism, hypothyroidism and adiposogenital dystrophia. Roentgen examination showed a tumor of the hypohysis and acromegalic changes in the bones of the hands. Endocrine disturbances occur too frequently in Reckinghausen's disease to be considered accidental. In this case the hormonal disturbances as well as all the cardinal symptoms of Recklinghausen's disease are, according to the author, a necessary consequence of a general cause, disturbance in the development of the ectoderm.

TRICHOPHYTIDS WHICH APPEAR ON SITES EXPOSED TO TRAUMA. D. W. NEKACHALOFF, Sovetski Vestnik Dermat. **9**:10 (Jan.) 1931.

A case is reported of congenital syphilis and trichophytia capilitii in a girl, aged 9 years, in whom an erythematous, scaly patch in the fold of one elbow developed several days after roentgen treatment of the scalp. For several days before the treatment the elbow had been exposed to wet dressings for an infiltration caused by the use of arsphenamine. A few similar lesions appeared a few days later on the trunk. From the scales of the lesions on the body, mycelia were present and *Trichophyton violaceum* was cultured, and from the hair, *Trichophyton album*. The author considers the lesions on the body as trichophytids, and thinks it possible that the wet dressings caused the fungi which were carried into the blood from the primary focus to settle in the fold of the elbow. The pathogenesis of trichophytids apparently depends not only on allergy, but on the biologic properties of the fungi.

PATHOLOGICO-ANATOMIC CHANGES IN THE MUSCLES, VESSELS AND VALVES OF THE HEARTS OF RABBITS IN EXPERIMENTAL SYPHILIS. K. IARISHEV, Sovetski Vestnik Dermat. **9**:22 (Jan.) 1931.

In 32 of 100 syphilitic rabbits, the author observed various changes in the histologic structure of the cardiac muscle. Different modes of infection were used: scrotal inoculations of passed virus (from one to forty passages) and intravenous, intra-ocular and congenital infections. The duration of the infection varied from five months to four years. There was no corresponding relation between the duration of the infection and the extent of the anatomic change. The pathologic changes consisted mostly in infiltration of muscular tissue with lymphocytes, fibroblasts and plasmocytes of Unna. The muscular fibers showed degeneration from swelling to rupture and fibrous changes. Three cases were of particular interest: one rabbit's heart showed a large circumscribed infiltration in the wall of the left ventricle which was composed mostly of epitheliod cells with a peripheral zone of lymphocytes and a narrow belt of fibroblasts and young connective tissue. In a second case there was a dense massive infiltration of plasma cells throughout the whole tissue of the left ventricle with considerable destruction of the muscle fibers. In a third rabbit true gummas of the human type were found with typical giant cells of Langhans, epithelioid cells and plasmocytes in a dense lymphatic infiltrate, with considerable alteration of the muscle fibers into coarse solid connective tissue. This was the only rabbit among 100 in which *Spirochetes* were found, spread throughout the dense lymphatic infiltrate and penetrating the walls of the coronary vessels which showed the picture of vasculitis obliterans.

SPONTANEOUSLY RECURRING ERUPTIONS CAUSED BY ARSPHENAMINE. B. KAPLUN, Sovetski Vestnik Dermat. **9**:31 (Jan.) 1931.

The author observed two cases of dermatitis due to the use of arsphenamine which recurred spontaneously. Through his own observations and those reported in the literature, he arrives at the following conclusions: 1. Eruptions caused by arsphenamine may reappear after complete disappearance and in spite of discontinuation of treatment with arsphenamine. 2. This condition is observed mostly in persons in whom the vegetative nervous system is damaged and in whom the liver does not function properly. 3. Constitutional peculiarities, congenital as well as acquired, play an important rôle. 4. Patients who have suffered from a dermatitis caused by the use of arsphenamine should not receive any arsphenamine for from three to four months in order that the arsphenamine and its products may be eliminated from the body. In the meantime, treatment for desensitization should be instituted. 5. In case it is necessary to administer arsphenamine earlier, great caution in dosage should be observed and prophylactic measures taken accordingly.

SYPHILIS AND CUTANEOUS DISEASES IN DAGESTAN. A. M. LEVIN and P. S. SAVINOFF, Sovetski Vestnik Dermat. **9**:37 (Jan.) 1931.

From 1924 to 1929, 45,045 natives of Dagestan were examined; of this number, 5,449 (12.09 per cent) were found to be syphilitic. Recent secondary and tertiary gummatous lesions prevailed. As to neurosyphilis, only one case of tabes was recorded. The percentage of people affected with cutaneous diseases varied in the different regions between 10 and 25 per cent. Pyodermias and scabies were seen most frequently. Fungous infections of the scalp, mostly favus, were found in from 4.5 to 8 per cent of the population; they affected particularly children about 15 years old.

THE DIAGNOSIS OF ULCUS MOLLE. I. MUNDER, Sovetski Vestnik Dermat. **9**:66 (Jan.) 1931.

The author employed the cultural method for the diagnosis of the soft chancre, using the medium of Nicolau and Bancu (1 per cent peptone water to which is

added one-fifth defibrinated blood). With this method he obtained a positive result in 45 per cent of clinically soft chancres, while with other methods, Ducrey's bacillus was found in only from 10 to 15 per cent of the cases.

THE USE OF BISMUTH IN THE TREATMENT FOR LUPUS ERYTHEMATODES. V. JACOBSON and K. BARKOFF, Sovetski Vestnik Dermat. **9**:68 (Jan.) 1931.

The authors report two cases of lupus erythematodes in which they gave a preparation containing quinine, bismuth and iodine injections. Although the history and the objective and serologic examinations of the patients gave results that were absolutely negative for syphilis, the effect of the treatment was excellent. The authors therefore advise the use of a preparation containing quinine, bismuth and iodine in the treatment for lupus erythematodes.

A CASE OF FOX-FORDYCE DISEASE IN WHICH A CURE WAS OBTAINED BY ANTISYPHILITIC TREATMENT. S. ARKANGELSKY, Sovetski Vestnik Dermat. **9**:70 (Jan.) 1931.

The author reports a case of Fox-Fordyce disease in a woman, aged 43, who had suffered for one year with severe pruritus in the axillae and around the right nipple. The past history revealed an insufficiently treated syphilitic infection. On physical examination, gastritis catarrhalis, vitium cordis, neurosyphilis and a clinically typical picture of Fox-Fordyce disease was found. The Wassermann reaction was strongly positive. Two courses of neoarsphenamine and bismuth were given, resulting in a complete cure of the disease. The author concludes that this dermatosis is only a symptom of secretory disturbances in the apocrine glands, which may be produced by many factors. BLOOM, New York.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

INDOLENT ULCER OF THE LEG. A. D. WRIGHT, Lancet **1**:457 (Feb. 21) 1931.

Wright treats indolent ulcer of the leg as follows: 1. The patient on first attendance has a history taken with a view to finding the cause. It is surprising how many have a history dating from typhoid, pneumonia, an operation, or a fracture. The ulcer is then mensurated with a celluloid grid and the circumference of the leg is measured. 2. The uppermost varicose veins are injected with sodium morrhuate in 5 per cent solution. The veins are always injected from above downward because the lower part of the leg is a locus minoris resistentiae and any mistake in injection is paid for in full. Deterred by an initial necrosis or severe reaction as a result of low injection, the inexperienced may abandon treatment and the patient may be left with his varicose veins and a chronic injection ulcer or indulent phlebitis. 3. The leg is then bandaged firmly and evenly over a longitudinal strip on both sides of the leg. When there is much edema, the bandage must be put on hard with practically all one's strength. The tightness is proportional to the swelling and induration, but one should always err in respect of being on the tight side. No treatment of any kind is applied to the ulcer, and eczema and phlebitis or periphlebitis are no contraindication. If the ulcer is of the painful malleolar type (Corlette's ulcer), the crater is filled with acetylsalicylic acid powder blown in with an insufflator. This is a valuable local analgesic. A sleeping powder may be given for the first week of treatment to ease pain and allay worry, and this secures the patient's confidence. Such a radical change of treatment is often likely to be contrary to the patient's own ideas on the management of ulcers and to be

met with some opposition at first. 4. The second visit is at a variable interval of from three days to a month, according to the size and position of the ulcer and the amount of edema. If the ulcer is large and its discharge copious, the bandage becomes sodden and requires frequent changing. If the edema is great, the bandage gets loose because of shrinkage of the leg and will require reapplication. If the ulcer is over the malleoli, the movements loosen the bandage and it has to be renewed more frequently. Sometimes if there is a marked degree of edema, an intravenous diuretic (mersalyl) is given. The patient on leaving is instructed to wash off the discharge with soap and a nail brush when it seeps through and put a dressing over the bandage. A free discharge must be regarded as beneficial. The patient is told to return to work, take plenty of walking exercise, and wear a long stocking or bandage over the adhesive to prevent it from being disturbed during sleep or in pulling on clothing. 5. At the second attendance the patient removes the bandage on arrival and wipes away the discharge with wet absorbent cotton. Again the veins are injected in the same order and, if the ulcer is large and a good sheet of granulations has developed, grafts can be inserted under the granulations on the fibrous bed of the ulcer. 6. Further attendances are at increasing intervals, and each time the visible and palpable veins are injected. Grafting may be repeated, and it is well always to have a graft waiting in the center of the last patch of ulcer to receive the edges as they close in; otherwise there is often an annoying delay at the last. 7. Finally, when the ulcer is cured and all veins have been obliterated, the patient is given an Unna's case or, better still, a Klebro resin bandage for three months to consolidate the cure. After this, permanent support may be required and this may take the form of a Klebro bandage renewed four times a year or an elastic stocking; of the latter, none is so effective as the Bourjeaurd. In seriously disorganized legs the support from any form of stocking is inadequate and firm Klebro, elastoplast or Unna bandages may have to be worn for some time. Patients are also seen every three months for injections and reconsideration as to renewal or abandonment of support. They are advised to wear boots instead of shoes, to cover every small abrasion with sticking plaster and to return if there is any recurrence.

EPILATION BY TWEEZERS IN DERMATOLOGY. R. SABOURAUD, Presse méd. **39**:113 (Jan. 24) 1931.

Sabouraud deplores the abandoning of the art of epilation by tweezers. This method of removing hair can never be entirely superseded by the use of roentgen rays. An application of rays is almost certain to leave a few scattered hairs in the scalp, which must be removed if the therapeutic effect is to be permanent. Moreover, many forms of tinea and other skin diseases require two or more depilations to effect a cure; and even a second application of roentgen rays may be dangerous, while a third is sure to be harmful. Many of the unsatisfactory results secured in the treatment for such skin diseases are due to the incomplete effects of the roentgen treatment, which could be admirably complemented by epilation with tweezers if hospitals and clinics had skilled epilators on their staffs.

BACTERIOPHAGE TREATMENT. P. HAUDUROY, Presse méd. **39**:168 (Feb. 4) 1931.

Hauduroy gives a discussion of the indications and method of application, both general and specific, of bacteriophagic treatment. He points out first of all the necessity of using a well prepared bacteriophage, since incorrect technic produces not only a useless medicament but one that is often dangerous and even fatal to the patient. Moreover, the bacteriophage used must be specifically lytic of the micro-organism causing the infection. Although it is not always possible to prepare the bacteriophage from bacteria secured from the patient, a test in vitro should always be made to determine the efficacy of the bacteriophage. The bacteriophage should usually be given in three or four subcutaneous injections

of 2 or 3 cc. each, at intervals of twenty-four hours. Five injections is the maximum that should be given to a patient under any conditions. Subcutaneous injections generally produce only slight local reactions and never cause general reactions. The injections should never be given in inflamed or painful tissues, since the results are no better, if as good, and the injections cause the patient unnecessary pain. Along with the injections, the bacteriophage should be applied in local dressings, adapted to the localization and form of the lesions. Intravenous injections should never be used; they have little therapeutic effect and cause dangerous shock reactions. The only types of infections in which the efficacy of bacteriophagic treatment has been established are staphylococcal and colibacillary. Bacteriophagic therapy is successful in all superficial or deep staphylococcal infections (provided the isolated micro-organism yields to the bacteriophage used) except staphylococcal septicemias. The resistance of the latter may be due to the fact that the treatment is usually necessarily given too late to be of value. The author has observed through his own experience and examination of the literature that about 75 per cent of cases of staphylococcal infection may be cured by bacteriophagic treatment. The reasons for the failure in some cases are obscure, undoubtedly owing in a great part to the "unknowns" of the physiopathologic conditions of the patient. In some cases in which bacteriophagic therapy alone was of no avail, the author used with it an autovaccine, with good results. In colibacillary infections one should make sure that the bacteriophage used is lytic of the isolated bacillus and that the infection is a pure colibacilluria, since many colibacillary conditions present complications that render the treatment useless.

PRURITUS VULVAE AS A RESULT OF PERNICIOUS ANEMIA. E. SCHULZE, Monatschr. f. Geburtsh. u. Gynäk. **87**:91 (Jan.) 1931.

After discussing the various causes of pruritus vulvae and the local changes of the skin, Schulze reports the case of a woman, aged 63. Because the patient's urine was found to contain sugar, it was assumed that the pruritus was of diabetic origin. However, even after the diabetic symptoms had been counteracted the pruritus was still of the former severity. Local medicinal treatment, baths and roentgen therapy were likewise without effect. The patient's general condition grew steadily worse; she lacked appetite and lost weight, and her face was pale yellow. Pernicious anemia was now thought of, and liver diet was instituted. The examination of the blood revealed a hemoglobin content of only 57 per cent and the number of erythrocytes was 2,890,000. After four weeks of liver diet the pruritus commenced to disappear and after three months the epithelial changes on the skin of the vulva had completely disappeared. The blood picture improved likewise. That the woman had had pernicious anemia, which led to pruritus vulvae, is proved by the efficacy of the liver diet.

ENCEPHALITIS AND GENERALIZED ERUPTION FOLLOWING VACCINATION. M. WEICHSEL, Monatschr. f. Kinderh. **49**:28 (Jan. 30) 1931.

In a child, aged 17 months, severe cerebral phenomena and convulsions suddenly occurred on the nineteenth day after inoculation with vaccine; left-sided hemiplegia complicated by spastic hemiparesis appeared. Simultaneously, vesicles developed on the chest, back, face, arms, neck and upper part of the right arm. The differential diagnosis from chickenpox was based on the aspect of the vesicles, their development near the inoculation pustule, and their simultaneous appearance. Moreover, the head and the mucosae were free from the eruption; there were no patients with chickenpox in the family. The differentiation from epidemic encephalitis was based on the fact that no such cases have been recorded, and especially on the absence of postencephalitic parkinsonism as well as of torsion spasms, obesity or epileptiform seizures. Weichsel ascribes the simultaneous appearance of the cutaneous and cerebral phenomena to an excessive formation of antibodies. Intratesticular injections of cerebrospinal fluid and corneal inoculations of the contents of vesicles were made in rabbits but the results of both tests were negative.

SUN RAYS COMBINED WITH ROENTGEN RAYS IN TREATMENT OF TUBERCULOSIS OF THE LYMPH NODES. K. MOSDZIEN, Strahlentherapie **39**:507 (Jan.) 1931.

Mosdzien considers a combined treatment of roentgen and sun rays as most favorable in cases of tuberculosis of the lymph node. The author treated 111 patients during the last two years; 64 were children and adolescents. In most of them the cervical lymph nodes were involved; in 16 the bronchial or the mesenteric lymph nodes. All adults, except one, presented tuberculosis of the cervical lymph nodes. The sun rays were provided by a quartz or by a carbon arc lamp. A marked pigmentation of the skin was avoided. The roentgen rays were passed through a copper filter; an aluminum filter was used when the diseased lymph nodes were superficially situated. From 150 to 190 kilovolts with from 4 to 6 milliamperes was employed. The rays were applied to two fields: the tube was placed sagittally on the anterior and on the posterior portion of the neck on the same side, thus including the whole involved region. The size of the nodes usually decreased after two or three irradiations each consisting of from 10 to 25 per cent of a unit skin dose. No more than three irradiations were employed; the interval between the first and the second irradiations was twenty days, and between the second and the third irradiations, four weeks. The results were good in the fistulous and ulcerous forms of the disease. A smaller dose of rays and an aluminum filter from 13 to 7 mm. thick were used in the ulcerous form; the scars were insignificant. The dose of rays used in the fibrous forms was one third of a unit skin dose; the intervals between the irradiations varied from six to eight weeks. In children, the dose of rays was a half or a third of the dose used in adults. In twenty-four cases the results from roentgen treatment alone were compared with those from roentgen rays combined with artificial sun rays. Favorable results were obtained more rapidly after the combined treatment. Surgical intervention is indicated in cases completely refractory to irradiations.

INOCULATIONS OF MALARIA FOR TREATMENT OF TABES. P. MINIOVICH, Klin. med. **8**:1085 (Oct.) 1930.

Miniovich used the treatment in seventy-five patients with tabes; in fifty-four of them, clinical and serologic observations have been continued from six months to two years. Forty-five of the patients were men and nine were women; their ages ranged from 24 to 58. The syphilitic infection was from five to thirty-six years' standing; in one, the disease was congenital. From 3 to 4 cc. of whole blood was injected intravenously or from 5 to 6 cc. subcutaneously. Malarial viruses of stock cultures conserved through continual reinoculations served for inoculation. The tertian type of malaria was chiefly used; the quartan type was employed in a few cases in which the patients appeared exhausted. The average of paroxysms to which the patients were exposed varied from twelve to fifteen; the minimal temperature was 39 C. (102.2 F.) and the maximal 41.8 C. (107 F.). Starting from the period of incubation, the patients were given cardiac stimulants. In case of intolerance to the malarial treatment, quinine in a dosage of from 0.05 to 0.1 Gm. was prescribed. In two patients the treatment had to be interrupted on account of signs of cardiac decompensation and on account of a severe jaundice and of a menacing general weakness in two and in one, respectively. In a series of patients with induced tertian malaria, the fever ceased spontaneously after from three to eleven paroxysms; if injections of milk failed to provoke further paroxysms and inoculation of malaria could not be repeated, typhoid vaccine was injected intravenously. The initial dose of the vaccine contained 50,000,000 bacilli; the dose was gradually increased. Injections of the vaccine were given twice a week; their total number amounted to from eight to twelve. There was a rise of temperature to from 39 C. (102.2 F.) to 40.8 C. (105.4 F.); the paroxysms of fever lasted from two to ten hours. The induced malaria was treated with quinine given by mouth; in cases of tertian fever, 1 Gm. of quinine was given daily for one week; in cases of quartan fever, 1 Gm. was given daily until the plasmodia disappeared from the peripheral blood, and was continued for five days.

In patients previously not treated and with a positive specific reaction, the malarial inoculation was preceded by a half or a whole series of arsphenamine and bismuth treatment. The specific treatment was renewed as soon as the malarial fever ceased; it was repeated at intervals of two or three months. In patients with a negative seroreaction, the preliminary specific treatment was omitted and one series of arsphenamine and bismuth injections was given after the malarial fever vanished. Of thirty patients with lightning pains, seventeen recovered, ten improved and in three the condition remained stationary. Sometimes lightning pains first appeared during the malarial treatment. The history of two patients indicated that lightning pains have disappeared for one and one-half and two years after natural malaria has developed. In two instances there was recurrence of the pains after a year. In three patients, gastric crises vanished after from ten to sixteen paroxysms of tertian fever, up to one and one and one-half years. The malarial treatment proved to be without effect in two cases of an extensive atrophy of the optic nerves. In twenty-nine of thirty-seven patients, positive seroreactions became negative or less intense; no changes were noted in eight. In eleven cases, positive Wassermann reactions of the cerebrospinal fluid became negative or less intense. Positive protein tests became negative in two and less intense in six; the number of lymphocytes in the cerebrospinal fluid returned to normal. Usually a positive mastic reaction persisted; in a few cases it became less intense. Improvement of serologic reactions occurred gradually, within about two years. Among sixteen patients with a pronounced ataxia, coordination of movements improved in six and the functioning of the bladder in three. In four cases paresthesia subsided, while extensive disturbances of sensibility remained unchanged. In three instances the patellar and the achilles tendon reflexes improved slightly; in others, they were not affected by the treatment. In two initial cases, anisocoria subsided and the reaction to light improved; in the remainder, the objective neurologic signs remained unchanged. In all, the malarial treatment was followed by a gain in weight of from 4 to 9 Kg.; the working capacity of many patients improved or even became restored. In cases in which reactions are negative and subjective signs are absent the malarial treatment may arrest the degenerative processes. The author suggests that malarial treatment be tried in cases in which the patients are young and the infection is recent; that is, when the prognosis for specific treatment is unfavorable.

TREATMENT OF ANTHRAX WITH LARGE DOSES OF SPECIFIC SERUM. L. CHEREMUSHKINA, Odessky med. j. **5**:295, 1930.

Cheremushkina's experience includes 115 patients with anthrax. A dose of 150 cc. of antianthrax serum was injected intravenously, on three successive mornings. On exception, the serum was injected also in the evening. It was warmed and injection was made slowly. In some cases, phenomena of serum sickness occurred, which lasted only a few hours. The local treatment consisted first in the application of dressings moistened with a 1:3,000 solution of corrosive mercuric chloride or with a 1:1,000 solution of potassium permanganate; later in the application of an ointment. The author stresses that antianthrax serum prevented the local infection from becoming general and it was frequently possible to cure an anthrax septicemia. The amount of the serum given may total up to a liter. In cases of medium intensity the serum is administered intramuscularly in a dose of from 80 to 200 cc.; the dose can be repeated. In severe cases the serum ought to be administered intravenously and intramuscularly (from 80 to 120 cc. at once). The action of the serum is probably antitoxic and bactericidal.

RESULTS OF AUTOHEMOTHERAPY IN CASES OF FURUNCULOSIS. A. BALMAGIYA, Vrach. gaz. no. 21, p. 1586, Nov. 15, 1930.

Balmagiya had used the treatment in ninety boys, aged from 10 to 17, pupils of a labor colony. In one group of thirty patients he used treatment with the usual remedies, among others, painting the furuncles with tincture of iodine,

applications of compresses with Burow's solution or of moist and hot poultices. Passive hyperemia and curettage, among others, were used when the furuncle was mature. In another group of thirty patients exclusive treatment with Besredka's antivirus was used, and in the remaining group autohemotherapy was tried. The treatment in the first group did not prevent the formation of new furuncles. In the second group also the effect of the treatment was insignificant. It also proved to be expensive and inconvenient, since the compresses should be renewed every four hours. For the autohemotherapy, the blood was withdrawn from the patient's ulnar vein and injected subcutaneously, usually in the subclavicular region. The blood became resorbed in two or three days; in rare cases the resorption was slow. The amount of blood of a single dose varied from 8 to 22 cc.; the total amount of blood injected varied from 8 to 90 cc. In moderate cases, the single dose of blood was from 10 to 20 cc.; in severe cases, the dose was increased to at least 15 cc. The injections were usually given at intervals of from two to four days. The autohemotherapy resulted in a rapid healing, sometimes within three days. The autohemotherapy was well tolerated; there were neither local nor general reactions. The author stresses the fact that the results were encouraging; besides, the treatment is within the reach of every one and therefore can be commonly used.

Society Transactions

ST. LOUIS DERMATOLOGICAL SOCIETY

MARTIN F. ENGMAN, JR., M.D., *Secretary*

Regular Meeting, Oct. 15, 1930

RICHARD S. WEISS, M.D., *Presiding*

RUMPFHAUT EPITHELIOMA. Presented by DR. ERIC BROCKELMANN.

Mrs. A. R., aged 56, had been in good health all her life except for enlargement of the lymph glands on both sides of the neck which had been present since she was 24 years old. On the left side of the neck there was a scar, the size of a finger-nail, which resulted from a broken down lymph gland at the time the patient was 24.

The present condition on her left hip began in the form of a red spot, the size of a pea, about ten or twelve years before presentation. The lesion gradually increased to its present size, that of a silver half dollar. Early in the present year, a lump formed inside of this area and a few similar lesions developed, until there was at the time of presentation a reddish, oval patch 3.2 cm. in diameter; it was sharply circumscribed, dry and scaly. On the lower border of this lesion there was an oval papillomatous growth, the size of a bean, 1.5 cm. in diameter and 3 mm. high.

On the right border of the abdomen there was a round, pale brown lesion, the size of a nickel, showing keloid-like elevations in the form of streaks between which depressed atrophic areas were visible. This lesion started the preceding winter from a "mole." At that time it was red and oozing, but later, it dried up and took on its present appearance.

Besides these lesions there were a few discrete, glistening, slightly elevated, pale brown, sharply defined patches, the size of a pea and larger, on the abdomen.

Biopsy of the nodule showed basal cell carcinoma. The Wassermann tests gave negative results.

DISCUSSION

DR. J. GRINDON: I should diagnose this as a case of Bowen's precancerous dermatosis; erythematoid basocellular carcinoma.

DR. W. H. MOOK: Clinically, I think that this is Bowen's disease.

DR. C. W. LANE: I believe that this is a case of multiple superficial epitheliomatosis, as named and described by Montgomery and as previously described by Wise and Fraser.

LUPUS ERYTHEMATOSUS WITH CARCINOMATOUS CHANGES. Presented by DR. HENRY C. SHAW.

L. S., white, aged 43, a housewife was admitted to the clinic of the Barnard Free Skin and Cancer Hospital, service of Dr. Engman and Dr. Mook, on Oct. 13, 1930. She presented sores behind the ears and a bald spot on the scalp. She was entirely well until two months before presentation when she was first troubled with itching behind the left ear. She noticed a small, hard, ulcerated area behind this ear. No treatment was applied. About a week later she discovered two similar areas behind the right ear, and two small, rough, scaly patches in each concha. The crown of the scalp also began to itch about this time, and hairs fell from a small scaly area in the vertex.

DISCUSSION

DR. W. H. MOOK: I believe that this is a case of lupus erythematosus and that the lesion over the left mastoid process has developed a carcinoma in the lupus patch.

EROSIO INTERDIGITALIS IN A NEGRESS. Presented by DR. G. V. STRYKER and DR. N. SCHLUETER.

I. S., a Negress, aged 39, employed as a dishwasher, came to the City Dispensary Clinic, dermatological service of St. Louis University, with lesions in the third interspace of both hands, and limited to that area only, of thirteen months' duration. The lesions were covered with a moist scale and surrounded by a collaret of epidermis, which was removed with difficulty. On removal of the scales from the base of the lesion, a smooth, red surface was revealed. The patient complained of itching and burning.

Examination of the scales in a solution of sodium hydroxide revealed many small oval yeastlike cells. A pure culture of round and oval yeastlike organisms was obtained on planting the scales in Sabouraud's agar.

This case was presented because it was unique in the presenters' experience in the colored race.

LICHEN PLANUS. Presented by DR. HENRY C. SHAW.

O. L., a colored woman, aged 24, a clerk, came to the Barnard Free Skin and Cancer Hospital, service of Dr. Engman and Dr. Mook, with a generalized eruption on the body. She stated that she had had a similar eruption on both legs and around the neck as long as she could recall, but that the lesions had caused no symptoms. About five years before presentation the eruption began to spread over the entire body, the individual lesions becoming larger, darker and scaly. Numerous Kahn tests gave negative results.

DISCUSSION

DR. W. H. MOOK: I treated this woman many years ago for lichen planus. In my opinion, the lesions on the mucocutaneous surfaces of the lips have been produced by an external irritation, probably from lip-stick. It is well known that lichen planus is prone to develop at a site of irritation or trauma. This is the most profuse development of lesions of lichen planus on the mucocutaneous surfaces of the lips that we have seen.

LICHEN PLANUS. Presented by DR. HENRY C. SHAW.

D. B., white, aged 51, a housewife, was admitted to the clinic of the Barnard Free Skin and Cancer Hospital, service of Dr. Engman and Dr. Mook, on July 15, 1930. She presented sore eyes and an eruption on the dorsal surface of both hands. The condition began about two months prior to presentation as a fine papular eruption which itched considerably. The individual lesions became larger, but the eruption did not spread. A week before the patient came to the clinic, the eyes had become red and inflamed.

A diagnosis of lichen planus was made, and treatment with the x-rays was begun, with marked improvement. On Aug. 7, 1930, she had a scaly itching eruption directly below the left axilla in an area about the size of a hand. The margin of this area was slightly erythematous and the center finely wrinkled and slightly darker in color. Scrapings were examined and cultured, but fungi were not found.

The patient was not seen again in this clinic until the present time.

DISCUSSION

DR. J. GRINDON: That keloid-like central condition and the purplish-red color around it in the left axilla suggest morphea.

A Case of Syphilis. Presented by Dr. Henry C. Shaw.

W. S., colored, aged 43, a laborer, was admitted to the clinic of the Barnard Free Skin and Cancer Hospital, service of Dr. Engman and Dr. Mook, in March, 1928. At that time he presented an eruption on the face, body and extremities, which had begun in 1926 on the eyelids and face as a papular eruption which coalesced to form large nodular masses. In the course of the following few months, a similar eruption appeared on the arms and trunk and in the popliteal spaces.

On examination the epitrochlear glands were enlarged, and the radial nerves were palpable. The Kahn reaction was four plus. Nasal smears were negative for Hansen's bacilli. The histologic examination was inconclusive.

The patient was presented to the St. Louis Dermatological Society in March, 1928, when a provisional diagnosis of syphilis or leprosy was made. He was given injections of mercury, but after treatment for two months he disappeared from the clinic and was not seen again until eighteen months later.

In February, 1930, he again came to the clinic, and there was practically no change in the type of the eruption. Intensive antisyphilitic treatment was begun with neoarsphenamine, and after four weeks the large nodular lesions were flatter, and the papules had disappeared. The patient complained of itching, and in the course of a few days there was a generalized desquamation. He was sent to the City Hospital where he was treated for exfoliative dermatitis for two months, and when seen again in the clinic there was complete involution of the large plaques, and only a few papules were present on the back.

He received two weekly injections of 65 mg. of mercuric salicylate, and the skin of the palms became dry and scaly. The antisyphilitic treatment was discontinued and sodium thiosulphate was given; the exfoliation disappeared. Two weeks previous to presentation the treatment was changed to carefully regulated doses of bismuth.

DISCUSSION

Dr. J. Grindon: Last June, Dr. Montgomery of Rochester, showed sections of undoubted syphilitic conditions with definite tuberculous architecture and everything that would make up a picture of a tuberculous lesion, except that in syphilis there is especial perivascular infiltration.

Dr. W. H. Mook: In most instances it is impossible to differentiate in the pathologic diagnosis between tuberculosis and syphilis from a slide, and it is only in the very earliest lesions, with a knowledge of the clinical history that the diagnosis may be positive. Judging from the amount of treatment with bismuth, arsenic and mercury, the therapeutic test would indicate that this is not a case of syphilis.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

A. Benson Cannon, M.D., *Secretary*

Jan. 6, 1931

Walter James Highman, M.D., *Chairman, in the Chair*

Keratosis Palmaris et Plantaris. Presented by Dr. Louis Tulipan.

W. C., a white boy, aged 12 years, weight 150 pounds (68 Kg.), whose mother and father were first cousins, was evidently suffering from a pituitary dystrophy (Frölich syndrome). His palms showed scattered pea-sized keratotic lesions. The heels and soles disclosed heavy, horny masses. All of the nails were dystrophic with hyperkeratosis and discoloration and curving.

DISCUSSION

DR. OSCAR LEVIN: The skin shows mainly keratotic lesions of the palms and soles with dystrophy of the nails. Other cutaneous evidences as well as signs in other structures suggest dysfunction of the pituitary gland. As a result of a cursory examination, I believe that the patient is suffering from Frölich's syndrome. The changes in the skin are merely external manifestations of the general condition.

DR. HERMAN SHARLIT: The patient is suffering from a pituitary dystrophy (Frölich's type), and patients so afflicted frequently present epidermal disturbances. While the keratotic patches on the palms and soles of this patient may not show the features looked for in cases of keratosis palmaris et plantaris, for instance, the distribution, they still remain keratoses of soles and palms, and must be so designated.

DR. GEORGE C. ANDREWS: I recommend surgical removal of the keratotic areas either with direct closure or with Thiersch grafts. I do not believe that any method that does not destroy or take away the basal cell layer of the affected areas will cure the condition. That skin must be removed and new skin put in its place.

DR. A. BENSON CANNON: I should doubt the diagnosis of keratosis palmaris et plantaris for the simple reason that there is no uniform distribution of the lesions on the patient's palms or soles as is invariably the case in this disease, in which I have never seen normal skin on the soles or the palms. In this case, the palms are apparently normal with the exception of two or three cornified plugs, and the soles are normal with the exception of a verrucose hyperkeratotic condition around the heels and a bit on the sides of the feet. I suggest that arsenic might be responsible for the lesions, especially as the onset occurred more than a year after birth. I suggest that the blood and urine be examined for arsenic.

DR. MAX SCHEER: Darier's disease, which may begin as early as the first and second year of life, should be considered.

DR. GEORGE C. ANDREWS: Each one who discusses the case seems to have his own diagnosis of this condition. Mine is ichthyosis hystrix.

DR. W. J. HIGHMAN: You mean in the sense of being a nevus?

DR. GEORGE C. ANDREWS: I mean in the sense of a congenital anomaly.

DR. LOUIS TULIPAN: This patient has keratosis of the palms and soles; therefore the disease is keratosis palmaris et plantaris. That is the only way to look at it. What is causing the condition is a different matter. The reason I presented this case is the factor of the parents' consanguinity; they are first cousins.

A CASE FOR DIAGNOSIS (PITYRIASIS ROSEA?). Presented by DR. MAX SCHEER.

B. S., a man, aged 27, a painter, born in Italy, from the Post-Graduate Skin Clinic, presented a generalized eruption that was most pronounced on the flexor aspects of the upper and lower extremities, the abdomen, the back, the scrotum, and the shaft of the penis. The condition began four weeks before presentation with a lesion on the inner side of the right elbow, which appeared as a red, pea-sized, scaly spot that had gradually increased in size until at presentation it was the size of a quarter. This lesion had a border that was one fourth inch wide, bright red, scaly and in places crusted. The center was clear. About a week after the appearance of the lesion, the rest of the eruption developed. This consisted of bright red, scaly patches from one fourth to 1 inch (0.6 to 2.5 cm.) and more in diameter. Some were oval, others circular; some had wrinkled centers typical of pityriasis rosea; others had a collaret and were somewhat fleshy, resembling a secondary syphilitic lesion. There were also some macules and scaly maculopapules on both palms. The rash had features of pityriasis rosea, secondary syphilis and disseminated tinea.

The Wassermann reaction was negative. The report of the examination for tinea had not as yet been received.

DISCUSSION

DR. EUGENE TRAUB: It is difficult tonight to make a positive clinical diagnosis of this eruption, but in my opinion the lesions on the palms of the hand are of a keratotic type seen commonly in psoriasis and rarely, if ever, in pityriasis rosea. The duration in this case is of no aid in a differential diagnosis. The patient presents a lesion on the arm that is said to have been the herald patch, but as there are other lesions of similar size on the arms any one of which might be interpreted as the mother patch, I would favor the diagnosis of psoriasis.

DR. CHARLES WOLF: I believe that this is a case of pityriasis rosea. There is a typical history of the herald patch on the right arm, followed by a free interval of ten days, and then an efflorescence of superficial, scaly, pink lesions, with the unusual feature of palmar lesions. I dare say these lesions will disappear by the time of the next meeting. I think that the patient should be presented again.

DR. M. B. PAROUNAGIAN: I regard the case as acute psoriasis. The location and bleeding point, after the nails have been scraped, would lead me to such a diagnosis.

DR. OSCAR LEVIN: I believe that I saw this patient about a week before presentation. At that time he showed a lesion, interpreted as a characteristic herald patch, and a disseminated generalized eruption. The unusual feature was that the condition involved the palms and extended up into the scalp. There was no evidence of psoriasis.

DR. MAX SCHEER: I presented this patient because the case is atypical. The largest lesion shown is the size of a quarter, with a clear center and well defined borders, simulating tinea. It is unusual to see a herald patch of this type in pityriasis rosea. Other unusual features are the lesions on the chest, the penis and the scrotum and the macules on the palms. One of the lesions was fleshy and suggested syphilis. For that reason a Wassermann test was made, with negative results. He has scurvy of the scalp.

A CASE FOR DIAGNOSIS. Presented by DR. HERMAN SHARLIT.

T. G., a white man, aged 35, stated that his present condition had started nine weeks prior to presentation with a coin-sized eruption on the inner side of the right arm. The lesion was described as a scaly patch. No other lesion appeared until two weeks later. At that time (when first seen by the presenter), an eruption appeared on the lower part of the trunk and on the arms consisting of discrete, scaly, pea-sized, erythematous papules. All of the lesions itched moderately and progressed to their present picture of grouped papules, forming annular and gyrate figures, scaling and itching and involving the axillae and groin as well as the areas first involved.

Examination for fungus gave negative results. Sections studied microscopically were described as pityriasis rosea.

DISCUSSION

DR. M. B. PAROUNAGIAN: I examined this patient carefully. The duration of the condition is said to have been between seven and eight weeks. The location of the lesions in the axillary and lower portions and on the extensor aspects of the body, and the characteristics of the lesions — patch formation and infiltrations — incline me toward a diagnosis of eczema seborrhoicum configuratum.

DR. OSCAR LEVIN: The lesions suggest those of pityriasis rosea. I agree with Dr. Sharlit's diagnosis. The unusual feature is the occurrence of most of the lesions on the abdomen.

DR. EDWARD R. MALONEY: We saw this patient many times at the clinic. Different diagnoses were made. Several dermatologists thought that the condition was pityriasis rosea, while others thought it acute psoriasis. A biopsy was taken, and the report of the histologic interpretation was that it was pityriasis rosea. After seeing the lesions a number of times in a good light, my impression is

that the condition is psoriasis. The lesions have continued for almost eight weeks without clearing up, and in spite of the histologic report, the diagnosis seems to me to be psoriasis.

DR. HERMANN FEIT: What interests me in this case is that it might be psoriasis. In examining the lesion one cannot find the characteristic changes one is accustomed to find in psoriasis. If the suggestions of Dr. Parounagian and Dr. Maloney are taken, we could compromise and call it psoriasiform seborrheic dermatitis (Unna).

DR. A. BENSON CANNON: I think Dr. Maloney's suggestion that this is a case of psoriasis is correct. The primary lesion is the size of a pinpoint, slightly raised, red and covered with a micaceous scale. On removal of this scale, bleeding points appear. I think that the large circinate type of lesion, with a clearing center and with micaceous scales at the borders, is merely the involution of the original primary pinhead-sized, elevated lesion.

DR. HERMAN SHARLIT: The evolution of the present status of the lesions in this patient was as given by Dr. Cannon. The lesions started as discrete, scaly papules which finally became confluent with the grouped lesions now present. In view of the histologic diagnosis of pityriasis rosea and the unusual distribution of the lesions now evident in the patient, we hesitated to accept the case as one of psoriasis. I now feel satisfied that the condition is psoriasis.

BASAL CELL EPITHELIOMA. Presented by DR. A. BENSON CANNON.

B. L., a woman, aged 26, married, born in New York, had consulted the presenter on Dec. 22, 1930, for a destructive ulceration of the nose of four and a half years' duration. The lesion had begun in the left nasal septum as a small pea-sized ulceration. The patient had been treated at various times for syphilis and for tuberculosis. She had received considerable roentgen treatment.

Examination showed a total destruction of the nose, with marked ulceration of the adjacent portions of the cheek and sloughing of the right cheek which extended almost to the corner of the right eye. At the left upper margin was a hard nodule the size of a large pea, pearly and with dilated blood vessels over the surface. The margins of the ulcer below this were nodular and of the same character. The skin over the upper lip was atrophic and telangiectatic. There was a foul odor to the necrotic ulcer.

Histologic examination of a nodule showed basal cell epithelioma. The Wassermann reaction was negative.

GRANULOMA ANNULARE. Presented by DR. A. BENSON CANNON.

M. H., a white girl, aged 4 years, had first been seen in the Vanderbilt Clinic on Dec. 12, 1930, with the complaint of an eruption on the right palm, the anterior surface of the ankles and the back, of three months' duration. There were no subjective symptoms.

There were several dime-sized lesions on the right palm, two similar ones on the back, one lesion the size of a quarter over the left ankle, and a pea-sized one over the anterior surface of the left ankle. The lesions had reddish, infiltrated, round areas with raised white borders and flattened, clearing centers. Similar lesions had since appeared on the left palm.

The Wassermann reaction was negative. The biopsy report was that of granuloma annulare.

DISCUSSION

DR. FRED WISE: The case is interesting from the clinical standpoint. Granuloma annulare occurs usually on the backs of the hands and in front of the ears. In this case the lesions are on the palms of the hands and there are no lesions on the face anterior to the ear. In children the clinical manifestations do not run true to form as compared to adults in whom the disease almost invariably appears on the backs of the hands. A number of cases of granuloma annulare in

children have been presented before this Section in which lesions appeared on the thighs and on other parts of the body without the characteristic clinical appearance of the disease on the backs of the hands, and yet, histologically, these eruptions were granuloma annulare.

The question arises whether this is a true example of that disease or whether it is an aberrant form of erythema elevatum diutinum. I do not know whether it is possible to make a definite microscopic differentiation between the two diseases.

Dr. Edward R. Maloney: I think that Dr. Wise covered most of the points in this case. I agree with the possibility of this case being one of erythema elevatum diutinum. The position of these lesions is unusual for granuloma annulare. Most of the lesions of this kind occur on the backs of the hands. It strikes me that in most cases of erythema elevatum diutinum there has been but one lesion. Here there are several. The two conditions are closely allied and it is hard to differentiate between them. I am inclined to think that this case shows a certain whitish elevated border which is more characteristic of granuloma annulare than of erythema elevatum diutinum.

Dr. A. Benson Cannon: The discussion has been very interesting, and I agree with everything Dr. Wise and Dr. Maloney have said. We called the condition granuloma annulare because it more nearly fitted this diagnosis than any one of the conditions belonging to the erythema group. As Dr. Wise mentioned, we all see cases of granuloma annulare in children that do not have the typical location and character that is found in the disease in adults. Although, histologically, the lesions may be identical in the two age groups, they often have dissimilar clinical characteristics and locations. I recall seeing a case several years ago with the late Professor Arndt in a child about 3 or 4 years old in whom the lesions were present only in the groin, yet clinically and histologically were granuloma annulare.

Trichotillomania. Presented by Dr. Leo Spiegel.

M. B., a white girl, aged 12 years, an American, had come to the Lenox Hill Hospital Clinic for the first time on the day of presentation. The patient's father said that she had been pulling out or breaking off her hair for the past two years. This desire had been uncontrollable and had apparently been getting worse. The eyebrows were similarly affected.

Examination showed patches on the scalp and eyebrows in which the hairs were broken off close to the follicular orifices.

DISCUSSION

Dr. Leo Spiegel: I saw this patient for the first time today. When I asked her how she took out her hair, she put the hair between the nail of the middle finger and the nail of the thumb and twisted the hair off. This is a compulsion neurosis, and should be considered with neurotic excoriations. She cannot resist the impulse, and there is no intent at deception.

Idiopathic Macular Atrophy. Presented by Dr. Max Scheer.

R. W., a woman, aged 21, had presented herself at the skin clinic of the New York Post-Graduate Hospital with several patches on the forehead and under the left eye. These areas were of one year's duration, were violaceous, situated slightly below the niveau of the skin and were atrophic. The lesions on the face resembled lupus erythematosus. At about the midportion of the right side of the back were several sharply circumscribed, slightly elevated and bluish-red, round, atrophic areas, the size of a small pea. A tentative diagnosis of idiopathic macular atrophy had been made. The pathologic report of Dr. Satenstein had read: "Edematous stage of macular atrophy" (from a biopsy of a lesion on the back).

DISCUSSION

DR. FRED WISE: I agree with the diagnosis as presented.

DR. HERMAN GOODMAN: I thought the lesions were erythematous and that the scar on the forehead was due to a former acne pustule. The patient takes phenolphthalein. It is my opinion that the eruption is due to this drug. There is no atrophy in the lesions on the face. The lesions on the back pointed out as atrophic do not fit in with my conception of idiopathic macular atrophy.

DR. M. SULZBERGER: This patient was treated at the Post-Graduate Hospital with gold sodium thiosulphate because the lesions on the face were considered to be a possibly atypical form of lupus erythematosus. They remained absolutely stationary under that treatment. The idea that the eruption might be due to phenolphthalein was considered and given up. The patient said that she had taken phenolphthalein eight months before presentation, but the lesions on the face and back do not clinically correspond to the usual picture of eruption due to this drug. The lesions are atrophic, and those on the back are best described as hernias of the skin. If you look closely you can also see atrophy of the macules on the face — the cigaret paper wrinkling. The color resembles that of Jadassohn's anetodermia maculosa which is a type of idiopathic atrophy. A biopsy was made and the histologic diagnosis was identical with the clinical one. The tuberculin reactions, which were performed in this case on account of the possible relationship of anetodermia with tuberculosis, were normal, being positive in a concentration of 1 : 5,000.

DR. W. J. HIGHMAN: Did the histologic examination include a study of the elastic tissue?

DR. MARION SULZBERGER: Yes, the elastic tissue was reported as partially absent.

DR. W. J. HIGHMAN: What is meant by the term "edematous stage"? Myxomatous degeneration occurs in von Recklinghausen's disease. It is unusual to find a combination of an edematous stage with an absence of elastic tissue, that is, with atrophy.

DR. MARION SULZBERGER: The biopsy report stated that there was considerable edema in the interstitial layers of the cutis and marked fragmentation of the elastic fibers.

DR. OSCAR LEVIN: I had an opportunity several years ago to study specimens from elevated and flat lesions of macular atrophy. The pathologic changes of both lesions were exactly alike. The apparent clinical edema is simply due to the fact that degeneration of the elastic tissue and relaxation of the skin with ballooning are present. I do not think that this can be called an edematous stage. It is all atrophy. The histopathologic changes do not simulate the myxomatous degeneration observed in fibroma molloscum. In view of the appearance of the lesions on the eyelid, one must bear in mind the possibility that this atrophy is due to atrophy from morphea.

DR. HERMANN FEIT: If the histologic report is disregarded, I think the diagnosis of idiopathic atrophy can be made clinically. The lesion is rather bulging in the skin.

PSORIASIS (FAMILIAL). Presented by DR. HERMANN FEIT.

The mother had died one year prior to the presentation of the two sons and one daughter, and according to the statement of an aunt, had always had psoriasis, especially on the head. Psoriasis had developed in all three children in early childhood. It was felt that dominant heredity was being dealt with, in which psoriasis had not been limited to either sex.

BASAL CELL EPITHELIOMA WITH METASTASIS. Presented by DR. HERMANN FEIT.

P. K., a man, aged 52, had always enjoyed good health up to six years prior to presentation, at which time he had acquired secondary anemia caused by chronic lead poisoning, which had finally forced him to give up his occupation as a chemist. In 1912, the patient had noticed a red spot on his back which had begun to scale and had grown from a nail-sized lesion to between 1½ and 2 inches (3.5 to 5 cm.) in diameter. When first seen by the presenter a diagnosis of Bowen's disease had been made, but the biopsy showed basal cell epithelioma. The lesion was desiccated and had been treated with filtered roentgen rays. While the patient was on a fishing trip in August, 1930, he had slipped and in falling, his left hip had struck against a rail. About six weeks later a lump had appeared in the left inguinal region.

At the time of presentation there was an atrophic oval-shaped patch over the sacral region about 1½ inches in diameter, the margin of which was hyperpigmented. In the left inguinal region was a hard mass about the size of a hickory nut. There was no history of syphilis, and repeated Wassermann tests had been negative.

DISCUSSION

DR. CHARLES WOLF: One may arrive at a diagnosis by a therapeutic test or histologic examination. I would suggest roentgen treatment, giving from a 50 to 75 per cent erythema dose, with copper and aluminum filtration. If the mass responds rapidly I would consider it either a lymphosarcoma or Hodgkin's disease. If the gland is excised, a histologic diagnosis may be arrived at. I do not think that there is any relationship between the present lesion and the lesion that was removed five years ago.

DR. FRED WISE: I think that in all cases of inguinal adenopathy associated with small penile lesions, especially when the patient is unaware of the existence of a penile lesion, a diagnosis of lymphogranulomatosis inguinalis should be considered and the Frei test should be made.

DR. W. J. HIGHMAN: It seems to me that to try to arrive at a rational conclusion concerning the value of roentgen treatment in causing disappearance of lesions on as flimsy a basis as this case presents is tenuous philosophy. The mere fact that lesions clear up does not indicate that the eruption is Hodgkin's disease or lymphosarcoma. Other types of lesions also disappear under such treatment. The penile lesion might readily account for the presence of swelling, whatever the local infection. If after due time no improvement takes place, I would have the gland examined microscopically.

DR. CHARLES WOLF: If this lesion was on the neck there would be no hesitation to resort to the suggestion I made. If you think it is an inflammatory gland, it is perfectly right to remove it. I do not think it is lymphogranuloma inguinalis. It is too firm and hard and has more of the characteristics of lymphoblastoma.

DR. W. J. HIGHMAN: If this lesion were on the neck, the lack of suspicion that it is related to the penile lesion might be justified. Since, however, this lesion is on the penis, the relationship of the gland must be excluded. We can wait to find out whether the patient has lymphosarcomatosis or Hodgkin's disease before any treatment is given; in the meantime I would let him alone.

DR. HERMANN FEIT: That the lesion is as hard as a rock can be determined by palpating it. The only way to determine the nature of the lesion is to have a biopsy performed. The patient has been suffering for many years from chronic lead poisoning. Lead is supposed to be a good remedy for carcinoma.

PARAPSORIASIS VARICELLIFORMIS. Presented by DR. ABRAHAM WALZER.

S. S., a woman, aged 23, single, a clerk, had had the present eruption for two weeks. The condition had started as a single "pimple" which within twenty-four hours had spread to the abdomen, extremities and upper parts of the thighs.

The lesions had begun as pinhead-sized, red papules, increasing in size and giving a lichenoid appearance. They were flat, red and some were varicella-like with central necrosis. The lesions were seen over the entire body, intermingling one with the other. With the disappearance of the varicella-like lesions, whitish scars had resulted, surrounded by erythema and in some instances by pigmented spots. There were no glands. The mucous membranes were free.

DISCUSSION

DR. BOLESLAW LAPOWSKI: I think that this is a case of varioliform pyodermia.

DR. FRED WISE: I agree with the diagnosis as presented by Dr. Walzer.

DR. EDWARD R. MALONEY: If there is such a disease I agree with the diagnosis. Recently a case was presented here showing a toxic eruption following the injection of tuberculin. It was diagnosed by some of the members as parapsoriasis varicelliformis. I do not see any reason why this case cannot be a toxic dermatitis due to some other toxin.

DR. CHARLES WOLF: I will agree with Dr. Lapowski if the lesions disappear in the next few weeks.

DR. W. J. HIGHMAN: If there is a disease of this sort, it would be better to call it exudative parapsoriasis; it is not varicelliform.

DR. EUGENE TRAUB: I think the most interesting phase of the matter under discussion is that within a period of about two years all of us have seen a number of these patients, while in the past I do not recall that any one saw this exact picture.

On March 25, 1930, I presented a patient before the New York Dermatological Society with a questionable diagnosis of dermatitis medicamentosa. The eruption in that case showed the early lesions presented by the patient tonight. On examination of the section, Dr. Highman suggested the diagnosis of pityriasis lichenoides chronica of Juliusberg. I have been able to follow this patient until the present time. The lesions run a definite course, beginning as small urticarial wheals or urticarial papules gradually flattening and becoming purpuric centrally, and as a final manifestation before they disappear, develop a scale with peripheral attachment. The individual lesions run their entire course in about three weeks, disappearing without scarring. Occasionally some slight pigmentation marking the site of an old lesion may remain for a long time, but this too eventually disappears. Apparently every one realizes that this must be either a new entity or an old disorder manifesting itself in an entirely different manner. At each meeting when a case of this type is discussed, unnecessary quibbling results concerning the name to be applied to this entity rather than a discussion as to its possible etiology and prognosis.

DR. ABRAHAM WAZLER: We must accept the fact that this patient shows a group of symptoms that make up a definite entity. This patient shows lichenoid and varicelliform lesions that will eventually lead to scarring. The eruption runs an acute course. To call it either parapsoriasis varioliformis or pyodermia is not as important as the fact that it is undoubtedly a definite entity. The objection to pyodermia lies in the fact that there are no pustular lesions. On the other hand, this patient does show lichenoid lesions as well as varicelliform lesions. Until we have a better nomenclature, descriptive names are still to be employed. Parapsoriasis varioliformis is therefore the most suitable name for this condition.

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. FRED WISE.

L. M., a boy, aged 19, presented himself at the skin clinic of the New York Post-Graduate Hospital with a complaint of swollen glands in the groin of two months' duration. The patient said that he had not had a penile lesion, but that he had intercourse with a woman who was a native of Porto Rico about three

weeks before the development of the inguinal adenopathy. The glands had grown progressively larger, and the patient had presented himself for relief.

In each inguinal region were masses of enlarged, hard, confluent, indolent glands. The skin overlying these glands was violaceous in color, not freely movable over the underlying glands and in the central area covered with a small crust. On removal of this crust, a thin seropurulent fluid exuded.

A small amount of pus had been removed by puncture of the gland and a vaccine prepared according to the method of Frei. The patient had then been tested intradermally with this autogenous vaccine and also with a similar vaccine from Breslau and some obtained from Copenhagen (Dr. Sulzberger). In forty-eight hours the intradermal injections gave the following results: at the site where the vaccine from Breslau was injected there was a small papule about three-eighths inch in diameter, elevated, edematous with a small amount of pus in the center. The skin was unbroken. The reaction to the injection of vaccine from Copenhagen was similar but milder, and the autogenous vaccine gave the mildest reaction of all. This in all probability was due to the fact that little material had been obtained from puncture of the gland.

DISCUSSION

DR. MAX SCHEER: Dr. Sulzberger made the test in this case and will tell us about it.

DR. MARION SULZBERGER: The clinical picture presented by the patient was one that could scarcely be diagnosed as anything but lymphogranulomatosis inguinalis, except for an atypical tuberculosis of the inguinal glands. It is unnecessary to describe the case. The bluish-red discoloration of the skin, the healed fistula and scarring, the hard masses of conglomerate glands with little fluctuation, the adherence of glands and skin are all typical. The Frei test is considered to be absolutely specific. If the vaccine is prepared with pus, patients afflicted with lymphogranulomatosis inguinalis give a positive reaction in forty-eight hours. I was fortunate to have two vaccines, one prepared by Hellesträm and one by Frei. Although all were old (over one year), they still proved active. That, I think, clinches the diagnosis. The interesting thing is that there are probably more cases of this kind in this country than we are aware of.

DR. JOSIAH THORNLEY: I have seen quite a number of these cases at the Hudson Street Hospital. We call them tropical buboes. I am under the impression that they are due to some organism getting into the cracks of the feet, for in the tropics sailors are in the habit of going about bare-foot.. We have had any number of patients in whom we examined the penis with great care and found no lesion. I think the original focus of infection is just as liable to be cracks in the soles as it is a penile lesion, which, when it is found, is so insignificant as to escape even the notice of the patient himself. To my mind, the infection, whatever it is, is superimposed on a slight abrasion on either the foot or the penis.

DR. A. BENSON CANNON: I have observed sixteen patients at the City Hospital and Vanderbilt Clinic each one of whom had a primary genital lesion. Often the initial sore was insignificant, causing the patient little, if any, annoyance, but after a few weeks would invariably develop an inguinal adenopathy followed by suppuration and the formation of sinuses. I have presented several of these cases before this Section. One of these was particularly interesting in that the patient had a generalized glandular involvement, the glands varying in size from an almond to that of an English walnut or larger, and an enlargement of the liver and spleen, the liver reaching almost to the pelvis. This patient made rapid improvement following radiation. I think lymphogranulomatosis inguinalis is decidedly more common than we suspect.

DR. FRED WISE: Did any of your patients have a stricture of the rectum?

DR. A. BENSON CANNON: No, none had stricture of the rectum.

DR. MARION SULZBERGER: The contention that lymphogranulomatosis inguinalis is a disease with a penile lesion or at least a venereal disease is supported in this case. It is rare in a temperate climate and is usually seen only in patients from the tropics or acquired through intercourse with people from tropical countries. The patient gave a history of intercourse with a Porto Rican woman three weeks before the appearance of the lesion.

A CASE FOR DIAGNOSIS (DERMATITIS EXFOLIATIVA?). Presented by DR. EUGENE TRAUB.

J. D., a man, aged 21, an American, a chauffeur, had first been seen on Jan. 5, 1931, at which time he complained of a generalized, dry, itching, scaly eruption of the skin. The condition had been present for two weeks, but the patient stated that he had had a few similar patches on his body for five years. These previous patches had caused no discomfort except for occasional mild itching. He had never had a generalized eruption nor had his face or hands previously been involved. The condition, so he stated, had begun as small wartlike lesions on the palms and backs of the hands, which had spread over the entire body and had become scaly and itchy. It had been accompanied at first by a tired feeling but by neither fever or other evidences of systemic disturbance. There had been a feeling of stiffness in the skin, and movement had been retarded and even slightly painful at time. The patient's general health, appetite, etc., had been excellent. He said that he had not used internal medication.

The previous history and the family history were unimportant. Physical examination gave negative results, except for a moderately inflamed throat, enlarged tonsils and carious teeth.

The condition consisted of a generalized hyperemic red skin with moderate infiltration and accentuation of the normal lines of the skin; extensive exfoliation of large, dry, silver-gray, superficial flakes, and sheetlike exfoliation on the palms. The scalp and hair were matted with scales. The face, scrotum and soles were free from scales. The lesions on the feet were more discrete and of papular type. The soles and toes were practically free from the eruption.

The Wassermann reaction was negative. Urinalysis showed a faint trace of indican. Microscopic examination gave negative results. The blood count showed: hemoglobin, 84 per cent; red blood cells, 4,250,000; polymorphonuclears, 67 per cent; lymphocytes 20 per cent; mononuclears, 6 per cent, and eosinophils, 7 per cent. Chemical analysis of the blood showed sodium chlorides, 433.5; sugar, 109.9; urea nitrogen, 13.3, and urea acid, 3.52.

On admission to the hospital the diagnosis had been exfoliating dermatitis of the Wilson-Brocq type.

DISCUSSION

DR. HERMANN FEIT: This is exfoliating dermatitis secondary to psoriasis. The changes in the finger-nails are typical of psoriasis.

DR. ADOLPH ROSTENBERG: A man who had known the patient for a good many years, said that he had not had psoriasis or any other skin disease previously. I agree that we are dealing with a true case of exfoliating dermatitis of the Wilson-Brocq type.

DR. W. J. HIGHMAN: Did you see anything signifying psoriasis?

DR. FRED WISE: There are a great many exfoliating and bullous skin diseases in which changes occur in the nails. I do not think that the idea that the so-called "thimble surface" or stippling is characteristic of psoriasis is now accepted. Cases of favus, eczema and ringworm are seen that have a form of stippling.

DR. BOLESLAW LAPOWSKI: I agree with Dr. Wise.

DR. HERMANN FEIT: The stippling of the nails in this case is characteristic of psoriasis.

DR. CHARLES WOLF: There were lesions on the foot that were strongly suggestive of psoriasis, and I, therefore, would be inclined to say that this is a case of secondary dermatitis exfoliative following psoriasis.

DR. MAX SCHEER: I would remind Dr. Feit that this subject was discussed about a year or so ago. A patient was shown with stippling of the nails and without lesions of the skin. The case was presented as psoriasis. I brought out the point that Dr. Heller stresses in his book, that there is only one characteristic psoriatic lesion of the nails, i. e., a scaly macule distinctly visible through the nail as a rosy red spot. It is very rare. All other lesions are secondary and may occur in other skin diseases.

DR. HERMANN FEIT: This was a case of mine that Dr. Scheer referred to. Later, typical psoriasis developed on the back.

DR. EUGENE TRAUB: As stated in the history, on admission, we considered the case one of exfoliating dermatitis of the Wilson-Brocq type. That diagnosis does not imply that the exfoliation was of primary or secondary type. Our case may be secondary to psoriasis, arsenic or any one of the possible secondary causes, or it may be one of a straight primary exfoliating type. At the present time, we are unable to determine what the patient's preexisting eruption might have been.

ERUPTION FOLLOWING INJECTIONS OF GOLD COMPOUNDS. Presented by Dr. A. WALZER.

F. J., a woman, aged 35, married, had had lupus erythematosus for about eight years. She was presented because several types of eruptions of the skin and mucous membranes had developed, following treatment with a gold compound.

The lesions of the mucous membrane had started with (1) a bad taste in the mouth after the second injection (total 0.10 Gm.); (2) the whitish appearance of the mucous membranes after the eighth injection and slight edema of the tongue and lips (total dose 0.7 Gm.); (3) lichenoid lesions on the cheeks, a vermilion border of the lip and tongue and lichenoid leukoplakia, and (4) vesicular lesions on the lips and tongue.

The eruption of the skin appeared as (1) erythematous irregular patches on both legs, pruriginous after the tenth injection (0.9 Gm. total amount received); (2) purpuric lesions and ulceration on the left leg, and (3) femorogenital lesions, erythematous annular patches without infiltration in the genitocrural region.

The lupus erythematosus lesions improved. The redness diminished and in some completely disappeared, but reappeared again in a more aggravated form. In all there had been no improvement regarding the lesions. The patient's general condition had changed also; she felt weak, with general malaise and a desire to vomit.

DISCUSSION

DR. ABRAHAM WALZER: Since the use of gold compounds in the treatment for all types of tuberculosis, certain manifestations have been noted in the skin following its employment. The term "aurid" has been employed in a sense comparable to the term "trichophytid." It implies first a sensitization to the substance—gold—and to the other fungi. The subsequent exposure to the sensitized substance produces lesions due to this sensitization.

This patient showed practically all of the types of manifestations in the skin that have been described following sensitization to gold compounds — pruritus, erythematous areas, purpura, metallic taste in the mouth, and lesions of the mucous membrane.

DR. ELIAS ABRAMOWITZ: Most authors reporting on the treatment for lupus erythematosus with gold compounds report some type of reaction as occurring occasionally with this form of therapy. Roxburgh and Corsi (*Brit. J. Dermat.* **42**:382 [Aug.-Sept.] 1930) treated thirty-five patients and encountered reactions in 6 per cent. It is not so much the preparation used as the dosage

that seems to account for some of the symptoms. It is for that reason that we seldom exceed 50 mg. of either triphal or gold and sodium thiosulphate in the treatment of our cases of lupus erythematosus at the Post-Graduate Hospital.

Eruptions of the mucous membrane of the mouth seem to be more common after the use of gold compounds than after that of the other preparations of heavy metals, such as arsenic, mercury, bismuth and thallium. Various types of dermatoses have also been reported after the use of gold compounds and are nearly analogous to those reported after the use of other metallic preparations. Wigley has detected the presence of gold in the eczematous patch that developed after the use of gold compounds for lupus erythematosus, but could not find it in normal skin, or in patients who tolerated the drug without any skin reactions (*Brit. J. Dermat.* **42**:405, 1930).

I believe that the French dermatologists were the first to apply the term "anti-pyrinids" in connection with antipyrin eruptions. To follow this through in addition to aurids, we would also have phenolphthaleinids, hydrargyrids, arsenids, thallids and bismuthids, etc.— terms that only express the cause of the eruption and leave the classification of the type of lesion produced out of the nomenclature.

MYCOSIS FUNGOIDES? Presented by DR. J. P. THORNLEY.

M. M., a man, aged 63, was born in Rumania; he was married and a painter. The family history showed that this mother had died of cardiac trouble; the cause of his father's death was unknown. One brother had died of high blood pressure. Three children were living and well. The previous history showed varicose veins and two operations for hernia. The patient said that he had not had venereal disease.

The patient's condition had begun six months prior to presentation with a patch of erythema in the left inguinal region, which had later become indurated and finally resembled a "small tomato."

On physical examination, the left inguinal region showed two large, purplish-brown infiltrated patches. The upper patch was the site of a tumor about the size of a small tomato which somewhat resembled the appearance of a tomato. In the left flank and under the right shoulder blade were small punctate pigmentations that seemed to follow the distribution of the intercostal nerves, over which were areas of which the patient occasionally complained because of itching.

The pathologist stated that the eruption showed a resemblance both to mycosis fungoides and to Hodgkin's disease.

PITTSBURGH DERMATOLOGICAL SOCIETY

JAMES H. FISCUS, M.D., *Secretary*

Meeting of Jan. 15, 1931

LOUIS WILLARD, M.D., *President*

LUPUS VULGARIS. Presented by DR. LOUIS WILLARD.

A man, aged 22, presented an eruption of closely set, yellowish-red, semi-translucent papules, posterior to the right ear. The involved area was soft and irregularly covered with nonadherent scales. Posteriorly, the advancing border was sharply defined and formed part of a circle. This, the oldest lesion, had begun when the patient was 4 years of age. The largest area was on the left arm; it was 10 cm. in diameter and in its center was a vaccination scar. The lesion

had appeared following an immunizing injection of diphtheria antitoxin in this area, when the patient was 6 years of age. Many smaller areas were scattered over the face, the trunk and the arms.

DISCUSSION

DR. STANLEY CRAWFORD: This was a typical case of an acute, inflammatory lupus vulgaris. All of the areas were studded with yellowish nodules that were soft and superficial, and the dull red congestion was an inflammatory reaction. No sign of lupus erythematosus was present, though the French idea of terming it lupus erythematodes because of the slight resemblance to lupus erythematosus might be used.

DR. G. J. BUSMAN: I should call this a typical case of erythematous lupus vulgaris.

MELANOMA. Presented by DR. C. B. NORRIS and DR. J. M. CAVANAUGH.

G. S., a man, aged 25, Arabian, presented a lesion of three years' duration on the dorsal surface of the right hand near the metacarpophalangeal joint of the middle finger. It was an elevated bluish-black lesion, about 3 cm. in diameter and 2 mm. in height. The surface was smooth and nonulcerating; the base was freely movable and unattached to the underlying structures.

The lesion followed a slight injury, and at this site a spot the size of a pea appeared that resembled a "blood blister"; it remained for about six months, but started to grow when the patient began to work. There was no history of a nevus in this area.

DISCUSSION

DR. STANLEY CRAWFORD: I should leave this condition alone or treat the lesion with radium.

DR. W. H. GUY: If the lesion has metastasized, amputation will not save the patient. Wide surgical excision is indicated.

DR. G. J. BUSMAN: I should search carefully for metastasis. If there is no evidence of this, I should amputate the arm.

DR. LESTER HOLLANDER: I should advise high amputation of the arm.

DR. H. T. PHILLIPS: I should perform a wide surgical excision of the local lesion.

DR. C. B. NORRIS: I agree that if metastasis has taken place, nothing will save this patient.

IMPETIGO WITH UNUSUAL HYPERPIGMENTED RESIDUA. Presented by DR. G. J. BUSMAN and DR. A. R. WOODBURNE.

M. R., aged 2 years, presented a group of serpiginous, hyperpigmented, circular lesions involving the lateral surface of the chest. On the fingers, elbows and knees, several typical, heavily crusted, impetiginous lesions were seen. This case was presented to show the unusual pigmentation following lesions of impetigo of rather long standing.

DISCUSSION

DR. LESTER HOLLANDER: This case was interesting in contradistinction to the patient whom I presented at the last meeting as having ecthyma followed by depigmentation.

DR. STANLEY CRAWFORD: Had silver nitrate been used?

DR. A. R. WOODBURNE: I thought that the slight scarring and hyperpigmentation was unusual. It was explained on the basis of an unusual pigmentary response, but probably the important point in this case was the difficulty that we had in getting the mother to remove the scales before applying an ointment. Silver nitrate was not used.

ERYTHEMA MANUS HEREDITARIUM. Presented by DR. G. J. BUSMAN and DR. A. R. WOODBURNE.

M. K., a white woman, aged 20, presented an eruption confined to the hands that consisted of a diffuse erythema that faded out gradually over the wrists. The ventral and dorsal surfaces of both hands were uniformally involved. There was no other eruption and there was no keratosis of the palms or telangiectatic vessels over the hands. The eruption had been present as long as the patient could remember. The general physical examination, the Wassermann test and urinalysis gave negative results. The basal metabolic rate was 17.5 per cent increased.

DISCUSSION

DR. C. B. NORRIS: My feeling was that this case was a vasoneurosis falling in the same category as erythema pernio.

DR. F. M. JACOB: This is usually a transitory condition in housemaids.

DR. LESTER HOLLANDER: I should investigate the condition as a trophoneurosis, especially in view of the fact that there was a definite thermic change; that is, the hands were cold and sharply above them, the skin of the arms was warm. The thyroid gland should be further investigated.

DR. A. R. WOODBURNE: I felt that this case resembled the cases that Dr. Lane reported as erythema palmaris hereditorum. As an etiologic agent one must consider a congenital absence of the sympathetic or an abnormal multiplicity of the deeper cutaneous vessels.

PARAPSORIASIS (?) Presented by DR. STANLEY CRAWFORD.

S. C., a white boy, aged 15, presented persistent, yellowish-red, rounded, macular lesions; a faint pityriasic scaliness of some of the lesions over the forehead, neck, the upper part of the chest, the forearms and the anterior portion of the wrists had been noted since birth. The father had the same eruption. A few varicella scars were noted on the trunk.

DISCUSSION

DR. A. R. WOODBURNE: I should consider this case lichenoid nevus.

DR. LESTER HOLLANDER: I also believe this case to be a nevus of the lichenoid type.

DR. G. J. BUSMAN: I should prefer to consider this case one of syringocystoma or a sebaceous adenoma.

LARGE NODULAR TYPE OF SARCOID OF BOECK OR NODULAR TUBERCULOSIS OF THE HYPODERM (WENDE). Presented by DR. LESTER HOLLANDER.

Mrs. C. C., a white woman, aged 26, an American housewife, presented a discrete and disseminated eruption involving the face, the neck, the arms and the legs. The eruption was composed of various sized, deep-seated nodules. The lesions varied in shade from red to bluish red; they were beefy and fleshy in appearance. The condition was of five years' duration. Two sections were examined, and the histologic picture was that of typical miliary and submiliary tuberculosis. Inoculation into a guinea-pig was performed on December 29. All other examinations gave negative results.

DISCUSSION

DR. STANLEY CRAWFORD: This is a most interesting case because of the widespread distribution of the lesions over the face, the arms and the legs. In some of the lesions the marked vascular dilatation was unusual. I think that treatment with arsenic should be beneficial. I was interested to see whether atrophy of the skin would follow the absorption of the lesions.

DR. H. T. PHILLIPS: These cases do not respond to arsenic as advocated by many authorities.

DR. LESTER HOLLANDER: The classification of sarcoid needs revision. Two types of conditions are included in this group, the tuberculous and the nontuberculous variety. For the sake of clarity, I believe that the name of the tuberculous lesions should be changed according to the name coined by Wende. This is important from the standpoint of treatment, as in my experience it is the nontuberculous type of sarcoid that responds to medication with arsenicals, while the tuberculous cases should be treated with tuberculin and autohemolytic therapy.

SARCOID OF BOECK. Presented by DR. LOUIS WILLARD.

A married woman, aged 62, presented on the middle of the forehead a slightly raised, violaceous red, rounded plaque 1.33 inches (3.38 cm.) in diameter and slightly harder than the normal skin. Neither scaling, scarring nor telangiectases were noted. Five other smaller and less developed areas were seen on the face. The lesion on the left cheek, which had appeared two and a half years previously, was of the greatest duration.

DISCUSSION

DR. W. H. GUY: The lesions on the cheeks suggested lupus erythematosis, and the lesion on the forehead was a hypertrophic lupus erythematosis in spite of the infiltration.

CUTANEOUS GANGRENE. Presented by DR. STANLEY CRAWFORD.

A. S., a man, aged 47, Polish, presented on the tips of the second, third and fourth fingers of the right hand and of the second, third, fourth and fifth fingers of the left hand, an old black, dry, leatherlike area of six months' duration, the result of a gangrenous process that involved only the capillaries of the skin. The process had formerly involved the second and third phalanges, but had diminished gradually until at the time the patient was presented only the tips of the fingers were involved. The condition appeared to be healing spontaneously. The outer surface of the right ankle showed a gummatous (?) lesion of eight weeks' duration. The plantar surface of the first toe on the left foot showed an irregular, dry, punched-out ulceration 2 cm. in diameter and evidently of a trophic nature. The pupils were static to light. The Wassermann tests of the blood and spinal fluid gave negative results. The cell counts of the blood gave normal results.

DISCUSSION

DR. W. H. GUY: The history did not state whether or not the patient had ever been frostbitten, but on questioning him it seemed possible.

DR. LESTER HOLLANDER: Two conditions occurred to me. The first was a toxemia due to ergot, suggested by the fact that the patient eats a great deal of rye bread. The second was an unusual type of pellagra.

DR. G. J. BUSMAN: I like to explain by one cause as many pathologic observations as possible. I therefore believe that the patient has a peripheral obliterative arteritis due to syphilis. He showed other tabetic changes.

DR. A. R. WOODBURNE: Has a roentgenogram of his toes been taken? As a rule, in thrombo-angiitis obliterans there is a marked rarefication of the bones.

DR. STANLEY CRAWFORD: This process was regarded as basically a vasoneurosis. It was true that the static pupil and the flaccid facies were indicative of tabes, but those observations in association with the coldness of the extremities, their rather blue color and a general hypotonicity of the entire skin favored the background of a neurosis. The patient stated that at one time his fingers suffered from severe cold, but that they were never frozen.

PARAPSORIASIS EN PLAQUE. Presented by DR. H. G. WERTHEIMER.

H. L., a white man, aged 45, married, presented an irregular generalized eruption of nine months' duration. The lesions were sharply defined, coin-sized patches, which showed a slight branny desquamation. The scales were somewhat adherent, but they could be scratched off without producing bleeding points.

DISCUSSION

DR. C. B. NORRIS: The lesions were superficial, scaly and associated with considerable pityriasis of the scalp. I felt that this condition was seborrheic dermatitis rather than parapsoriasis.

DR. LESTER HOLLANDER: Within the lesions there was telangiectasia, which made me consider the diagnosis of lupus erythematosus.

DR. G. J. BUSMAN: I do not believe that this case belongs to the class of lesions as presented. The eruption was not bluish or orange. Below the knees it had the character of psoriasis; elsewhere it was more of a seborrheic dermatitis.

SARCOID: DARIER-ROUSSY. Presented by DR. F. P. KENNEY.

C. S., aged 45, a white woman, from the department of dermatology, University of Pittsburgh, presented subcutaneous pea-sized nodules the distribution of which was limited to the chest, the back and the arms. They disappeared spontaneously and left an atrophic area under the skin. The patient had arthritis with rheumatic nodules on the fingers. This condition had been present for two or three years. The patient refused a biopsy.

DISCUSSION

DR. G. J. BUSMAN: I should want to know the results of a biopsy and of a Wassermann test, etc., before concurring in the diagnosis.

DR. LESTER HOLLANDER: I cannot offer a better diagnosis than the presenter. The lesions began as subdermal nodules that were followed by absorption and scarring. I believe that a biopsy should be done.

DR. W. H. GUY: When resolution takes place these nodules leave deep depressions, but no changes in the overlying skin.

DR. F. P. KENNEY: I will do a biopsy if the patient permits it.

ROENTGEN (FILTERED) DERMATITIS OF ABDOMEN. Presented by DR. STANLEY CRAWFORD.

Mrs. M. K., aged 52, presented a large, round, deep-seated infiltration, about 15 cm. in diameter and at least 4 cm. in thickness, on the lower part of the abdomen below the umbilicus. Centrally there was a rounded ulceration 5 cm. in diameter, the edges of which were pale and sloping and enclosed a foul-smelling, grayish-black, necrotic mass apparently 3 or 4 cm. in diameter. Beyond the ulcer, the deep, firm infiltration extended for 5 cm. in every direction, covered by apparently normal epidermis. The whole lower part of the abdomen showed hyperpigmentation with straight margins from the shielding of the distal areas from the rays. Biopsy showed a normal epidermis and a fairly normal papillary portion of the corium; the lower part of the corium showed swollen, pale and hyalinized connective tissue. The lower portions of the buttocks showed hyperpigmentation with deep areas of indurative edema of the lymphatics. The patient had received filtered, high voltage treatments with the roentgen rays at weekly intervals for several months at a time, during the past year, for uterine bleeding, the uterus being irradiated from all angles. The case was undoubtedly one of roentgen necrosis of the deeper tissues of the lower part of the abdomen without involvement of the epidermis except in the central ulcerated area. The treatment considered was excision of the entire mass.

DISCUSSION

DR. EMERSON GILLESPIE: I thought that this condition looked like a necrosis due to irradiation. The patient gave a history of having received roentgen therapy for uterine bleeding; the treatments had been given at weekly intervals for one year. There is a sharp margination of the erythema where the lead was laid across the abdomen.

DR. LESTER HOLLANDER: I believe that the observation of Dr. Gillespie is only partly correct; the patient does show a burn caused by the roentgen rays, but in addition the large granulation might be due to diabetes mellitus or to a large gumma. One knows how frequently gummas localize in traumatized areas.

DR. H. G. WERTHEIMER: I do not believe that the burn was caused by the roentgen rays, as this amount of destruction would be painful. I should not care to venture a definite diagnosis at this time.

DR. STANLEY CRAWFORD: Clinically, there were many signs that the condition is a gumma, but the dense infiltration is an inflammatory reaction following the irradiation. The entire mass might be removed by complete excision.

ERYTHÈME ANNULARE CENTRIFUGE. Presented by DR. LESTER HOLLANDER.

Mrs. M. C., aged 53, an American, presented an eruption that affected the trunk, the lower abdominal region and the upper portion of the lower extremities. The eruption consisted of nonpruriginous, flat, reddish, gyrate, slightly desquamating areas which were chronic and which usually began from a small rounded maculo-papule. The eruption was of three years' duration; it tended to fade and then to reappear. Laboratory examinations gave essentially negative results, with the exception of a hypochlorhydria as evidenced in two gastric analyses. On January 5, the total acidity was 3, the free hydrochloric acid, 0 and the combined hydrochloric acid, 3; on January 12, the total acidity, 6, the free hydrochloric acid, 2 and the combined hydrochloric acid, 4. The basal metabolic rate on January 12 showed a 31 per cent increase.

DISCUSSION

DR. H. G. WERTHEIMER: I believe that this case is one of seborrheic dermatitis. There is marked scaliness of the scalp and yellowish-red, soft, scaly patches over the body. In erythème annulare centrifuge the lesions are usually bluish-red, crescentic or annular patches with raised borders.

DR. G. J. BUSMAN: This patient had seborrheic dermatitis. The seborrhea of the scalp, the oozing behind the ears and the erythematosquamous lesions over the flexures and various areas of the trunk, lead me to regard this as a seborrheic dermatitis. The patient is obese and is a typical host for this condition.

DR. LESTER HOLLANDER: I presented this case under the diagnosis of erythème annulare centrifuge because it resembles the third case in the group that Dr. Graham and Dr. Throne presented in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**22**:777 [Nov.] 1930). The lesions began as small nodules that spread peripherally and formed gyrate figures. This case may be one of toxic erythema.

TERTIARY SYPHILIS. SARCOMA? Presented by DR. CLAUDE B. NORRIS.

H. H., a white American, aged 50, married, presented on July 14, 1930, a swollen, dusky red, circinate ulcer at the inner part of the right malleolus. Nearby there were one or two pea-sized subcutaneous nodules. The Wassermann reaction of the blood was 4+. Treatment was instituted on July 21, and within eight weeks the aforementioned lesion had disappeared. On September 13, a large nodule was noted on the anterior aspect of the right shin; above this there was also a smaller one. Later two or three more nodules appeared which seemed to follow the course of the popliteal artery or the sciatic nerve. All of these nodules

were regarded as syphilitic; their growth was rather slow for several weeks, until ten days before presentation it was found that the large nodule on the shin had doubled in size, and that the others were enlarged proportionately.

On Jan. 5, 1931, the following dose of roentgen rays was given: 5 milliamperes of current, an 8-inch (20.32 cm.) spark gap and five minutes' exposure at a distance of 8 inches, an aluminium filter of 2 mm. being used. On January 10, the aforementioned dose was repeated. Within the five-day interval, the involutionary change was very marked.

This case was presented to confirm the diagnosis of sarcoma, if that was correct, and to call attention to the coexistence of the two conditions, both of which are grave, the one not being recognized because of the preponderance of the other.

DISCUSSION

DR. G. J. BUSMAN: I believe that the iodide compounds are a factor in the production of the large lesion on the shin. The patient stated that when administration of the "drops" was discontinued and treatment with roentgen rays started, he showed improvement. It might be well to try the intravenous administration of sodium chloride.

DR. W. H. GUY: A histologic examination would be necessary to establish a diagnosis. The type of the granulomatous mass seen over the shin suggested a tuberculous process. While the mass seemed too soft for a lesion due to bromide or iodide, one of the halogens may be to blame.

DR. LESTER HOLLANDER: I consider this eruption due to a drug.

DR. C. B. NORRIS: It seems improbable that the eruption was due to some halogen, such as the iodides. The patient was and is still receiving sodium iodide, it is true, but the lesions have involuted rapidly under roentgen therapy. That this improvement would result in the presence of continued use of the drug seems to me to be unusual. On the other hand, I cannot definitely dispute the fact. Subcutaneous nodules, such as these, may occur from the iodides. I had never seen a case of the sort before. One of these nodules was present at the beginning, but it was very small. A biopsy would settle the matter.

ACANTHOSIS NIGRICANS. Presented by DR. F. AMSHELL.

C. P., a girl, aged 11½, was seen for the first time on Oct. 30, 1930. She presented a verrucose eruption on the back of the neck; it ranged in color from a dark brown to slate and was of a velvety texture. The lesion had been present for two years and was gradually becoming worse. During the past three months the lesion had become lighter in color.

DISCUSSION

DR. B. A. GOLDMAN: I suggest the diagnosis of nevus unis lateralis in a darkly pigmented person.

DR. G. J. BUSMAN: I should search for pediculosis capitas.

DR. W. H. GUY: I could not agree with the diagnosis presented. I felt that the condition lacked all the cardinal signs. Without a biopsy I should not offer a diagnosis.

DR. A. R. WOODBURNE: If there are no more extensive lesions in other areas, I should consider this a verrucose type of nevus.

DR. F. AMSHELL: The eruption is not pruritic, and there is no evidence of pediculosis capitis. Under treatment with a strong salicylic acid and an ointment of ammoniated mercury diligently applied, the eruption has become much lighter and not so verrucose. I still feel that this is a case of acanthosis nigricans.

SCLERODERMA. Presented by DR. CLAUDE B. NORRIS.

K. M., a woman, aged 28, married, presented pigmented and white lesions extending over several areas of the trunk. The older or pigmented lesions were oval or round in outline; the borders were not definitely limited and showed central atrophy. These older lesions had first appeared as white spots when the patient was 11 or 12 years of age, at which time a physician gave her some form of treatment with light; immediately following this treatment the lesions became pigmented and remained so. The newer lesions presented firm, ivory-colored central areas, the firmness lessening toward the periphery. The patient had a tendency to become obese; some thyroid change had been suggested by her physicians and for months she had taken 0.5 grain (0.0324 Gm.) of thyroid extract three times a day. No laboratory examination had been made.

DISCUSSION

DR. G. J. BUSMAN: The lesions have shown excellent response to therapy, as most of the spots are merely pigmentation.

CASE FOR DIAGNOSIS. Presented by DR. G. J. BUSMAN and DR. A. R. WOODBURNE.

S. A., a woman, married, aged 34, presented two granulomatous lesions of the right breast to the left of the nipple. The lesions were sharply marginated, circular, raised and slightly verrucose or papillomatous. There were a few small miliary abscesses in the lower lesion. There was scarring from supposedly similar lesions above and below the nipple. The onset followed abscesses of the breast which developed while the patient was nursing her last child three years before examination. The Wassermann reaction of the blood was negative. No specimen for biopsy was taken.

DISCUSSION

DR. STANLEY CRAWFORD: This was bromoderma because of the dull red, infiltrated, slightly papillomatous and verrucose character of the lesion and the association with the history of having taken a nerve sedative for many months.

DR. W. H. GUY: I felt that this case was a blastomycetic dermatitis.

DR. LESTER HOLLANDER: I thought that this condition was tuberculosis verrucosa cutis because of the color, the infiltration and the verrucose character of the lesions.

DR. G. J. BUSMAN: We intend to do a biopsy when we are permitted.

LICHEN PLANUS. Presented by DR. CLAUDE B. NORRIS.

C. W., a man, married, was first seen on Oct. 19, 1930, at which time he presented two lesions on the shaft, one lesion on the glans penis and also lesions on the mucous membrane of the mouth. On the penis there were three ringlike lesions; the borders were slightly raised and fairly firm, and the centers were depressed, violaceous, free from vesiculation and without a tendency to scale. Considerable pruritus was present. The Wassermann reaction was negative.

The patient has been given treatment with the roentgen rays administered locally to the lesions, and spinal irradiation was also given. Local applications of mercury and mercuric salicylarsenate administered intramuscularly were given. The patient had made some slow progress, and was shown for suggestions as to treatment.

DISCUSSION

DR. H. T. PHILLIPS: I believe that mercury is of more value than arsenic.

DR. C. B. NORRIS: I also feel that mercury is really of more value. This patient has been given twenty-two injections of mercuric salicylarsenate at biweekly

intervals and shows no definite improvement. Regarding the use of roentgen therapy over the cervical and sacral spinal areas, it has been my experience that the method is of value in acute cases but not in chronic cases such as this or in the hypertrophic type.

DETROIT DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Jan. 20, 1931

C. K. VALADE, M.D., *Presiding*

A CASE FOR DIAGNOSIS (DERMATITIS MEDICAMENTOSA [NEOARSPHENAMINE]?). Presented by DR. C. K. VALADE.

E. W., a married man, aged 30, who was unemployed, had been a rubber worker, operating a tire-making machine, until July, 1930. In March, 1930, following an occupational abrasion of the left arm, an eruption had appeared on the arm and around the waist which lasted for three weeks. In October, a scaling dermatitis had appeared on the right thumb. The condition was treated for two months as dermatophytosis; it had improved temporarily, and it recurred on December 18, together with an undermining paronychia of the third finger. Soon after this, an eczematoid dermatitis had appeared on the right arm and left leg, rapidly extending and involving the face and both upper and lower extremities. The eruption was vesicular and erythematous, with an offensive odor, and it was intensely pruritic. A scaling eruption had then appeared on the toes. The condition had persisted, practically unchanged.

Since 1929, when the Wassermann reaction had been found to be strongly positive, the patient had received three courses of neoarsphenamine and mercurial preparations, and a mercurial course was being given at the time of presentation. The last two Wassermann reactions had been negative. A biopsy had been made.

DISCUSSION

DR. A. P. BIDDLE: The eruption is probably of occupational origin, possibly being aggravated by some other cause.

DR. R. C. JAMIESON: I saw the patient two weeks ago, and I felt that the eruption might be a dermatophytid. I have observed a similar eruption due to sensitization to oatmeal.

DR. L. W. SHAFFER: Antisyphilitic treatment might have something to do with this condition. However, it may be a peculiar toxic dermatitis, such as we have observed recently, at first resembling pityriasis rosea and later becoming diffuse and generalized, with an acute course and early recovery.

DR. C. W. BEHN: I observed a similar case that developed in a rubber worker from contact with hexamethylenamine, the etiology being proved by patch tests. Antisyphilitic treatment may have aggravated the condition.

DR. C. N. MEYERS (New York): This dermatitis is apparently due to the accumulation of arsenic and mercury. Urbach has demonstrated the retention of large quantities of chlorides in the tissues, and there is a high icteric index.

DR. H. J. PARKHURST: Stokes, in his book on clinical syphilology, emphasizes the necessity of avoiding irritation of the skin of patients who are receiving the arsphenamines. The occupational irritation may have precipitated the outbreak in this case.

DR. C. K. VALADE: How late after the administration of the arsphenamines has arsenical dermatitis developed?

DR. C. N. MEYERS: Seven years later, in one case of which I know.

DR. R. C. JAMIESON: I have never seen a dermatitis of this type due to arsphenamine. Why should the cases occur so seldom? The patient may have inhaled some toxic chemical substance at the rubber factory.

DR. A. E. SCHILLER: This condition may be an industrial dermatitis, and it may be complicated by a dermatophytid. The lesions on the toes are indicative of dermatophytosis.

DR. C. A. DOTY: About three years ago I observed a similar case in a rubber worker who was sensitized to aniline. This eruption may be occupational.

ADENOMA SEBACEUM. Presented by DR. A. E. SCHILLER.

P. S., a youth, aged 18, presented numerous papules in the central portions of the face, ranging in size from that of a pinhead to that of a small pea and varying from the color of skin to brownish red. There were a few small telangiectases on some of the lesions. Several of the lesions were discrete, while others were confluent. The condition had been present since early childhood.

PITYRIASIS ROSEA (?) AND SYPHILIS. Presented by DR. W. G. SAUNDERS.

Mrs. E. C., a Negress, aged 22, had one living, healthy child, aged 3, and had not had a miscarriage or a stillbirth. She presented an extensive, intensely pruritic, maculosquamous eruption, involving the trunk, arms, hands, thighs and upper portions of the legs. Many of the lesions showed cigaret-paper crinkling. The Wassermann reaction of the blood was strongly positive.

DISCUSSION

DR. A. P. BIDDLE: The oral lesions are suggestive of syphilis.

DR. H. L. KEIM: I, too, found mucous patches in the mouth. The nature of the eruption was not so clear. It may have been a macular syphilid undergoing involution.

DR. A. E. SCHILLER: Might not an intense toxic erythema produce these oral lesions?

DR. H. L. KEIM: I do not believe that it would produce this amount of infiltration.

DR. G. W. HYDE: There is a general shotty lymphadenopathy.

DR. R. C. JAMIESON: The exanthem was intense and occurred mostly between the shoulders and knees, which would favor a diagnosis of pityriasis rosea. If it were an early syphilid, it should have been more generalized.

A CASE FOR DIAGNOSIS (LICHEN PLANUS?). Presented by DR. C. K. VALADE.

Mrs. M. T., a Negress, aged 27, presented a pruritic eruption of two months' duration. On the inner aspect of each foot were small, flat papules with whitish striations and sharp borders. There was a somewhat infiltrated lesion on the left elbow, with a depigmented border.

DISCUSSION

DR. L. W. SHAFFER: There are several possibilities: sarcoid, lichen planus and an eruption due to phenolphthalein. A biopsy will be needed to settle the diagnosis.

DR. E. C. TROXELL: There are lesions of lichen planus in the mouth.

DR. H. J. PARKHURST: I agree with the diagnosis of lichen planus. The oral lesions seem characteristic.

NEVUS PIGMENTOSUS. Presented by DR. JOHN H. BESANCON.

T. B., a man, aged 23, presented a flat, pigmented nevus, with verrucous portions, extending over the entire pubic region. The nevus was a very dark brown. It had been present since birth. Suggestions for therapeutics were asked.

DISCUSSION

DR. A. P. BIDDLE: The nevus is too deeply pigmented to warrant the risk of attempted removal.

DR. C. K. HASLEY: I should advise letting the lesion alone.

DR. C. W. BEHN: At Harper Hospital we have found that if such cases are left alone, a malignant condition may develop later; however, if the patients are treated, a malignant process may be precipitated.

A CASE FOR DIAGNOSIS (PITYRIASIS ROSEA?). Presented by DR. R. S. DIXON.

L. M., a girl, aged 19, presented an apparently fading, brownish-red, somewhat pruritic, macular eruption on the trunk, thighs and forearms. There were hemorrhagic elements in some of the lesions on the thighs. The visible mucous surfaces were not involved. Feenamint has been used for some time for relief from chronic constipation.

DISCUSSION

DR. A. E. SCHILLER: The condition may be pityriasis rosea, but there should be more involvement of the trunk and arms.

DR. H. J. PARKHURST: The eruption has the appearance of pityriasis rosea that is undergoing slow involution. The lesions on the thighs, some of which are hemorrhagic, were the last to fade, which would account for the apparently peculiar distribution.

DR. R. H. STEVENS: I found lesions characteristic of pityriasis rosea on the arms and trunk.

A CASE FOR DIAGNOSIS (PRICKLE CELL EPITHELIOMA?). Presented by DR. R. S. DIXON.

G. T., a woman, aged 27, had first noticed several hard papules in the natal cleft three months previously. There had been moderate pruritus. Superficial ulcers had formed, with a serous exudate. They had gradually enlarged to the size of a coin, becoming cup-shaped, and the surrounding tissue was red and indurated. Local applications were not beneficial. On biopsy, a pathologist had found a few epithelial pearls, and he had made a diagnosis of prickle cell epithelioma.

DISCUSSION

DR. C. K. HASLEY: The multiple lesions are probably tuberculous rather than epitheliomatous.

DR. L. W. SHAFFER: I favor a diagnosis of tuberculosis verrucosa cutis, especially since the patient has had fistula in ano. When the biopsy was made, some of the papillae might easily have been sectioned, leading to an erroneous diagnosis of prickle cell epithelioma.

ULERYTHEMA OPHRYOGENES AND SYPHILIS. Presented by DR. R. C. JAMIESON.

Mrs. K., aged 60, who was born in England and gave an apparently irrelevant past and family history, had been treated for lupus vulgaris for thirty years. There was a soft, pliable, circinate scar, apparently syphilitic, on the left leg, and a more recent, reddened, serpiginous and circinate scar, with some formation of keloid, on the left shoulder. The latter might have followed lupus vulgaris.

On the left ear there were a number of small ulcerating nodules, tending to coalesce, of three or four months' duration. In the eyebrows and over the entire scalp there was an extensive erythematous process, with a reticulated atrophic network of scar tissue. This last condition was of thirty years' duration, having extended gradually. The Wassermann reaction of the blood was strongly positive.

DISCUSSION

DR. R. C. JAMIESON: I think that the scars on the back are unusually keloidal for a syphilitic process.

DR. H. L. KEIM: I believe that the condition is mostly syphilitic.

DR. H. J. PARKHURST: I should expect to find ulerythema ophryogenes associated with tuberculosis rather than with syphilis; therefore, I think that the patient has both cutaneous tuberculosis and syphilis.

SCLERODERMA. Presented by DR. C. K. HASLEY.

E. E., a girl, aged 11, had been presented before the Society in November, 1930, and the case was reported in the proceedings in the ARCHIVES (**23**:586 [March] 1931). She was shown again to illustrate improvement following treatment with thyroid.

DISCUSSION

DR. A. E. SCHILLER: Previously, the patient had been treated with typhoid vaccine administered intravenously and with ultraviolet rays, without benefit.

DR. C. N. MEYERS: I have been interested in scleroderma for ten or twelve years. Ayres found pathologic quantities of arsenic in the urine, and one must consider this possibility in every case. In New York we have controlled our medication with thyroid with estimations of the basal metabolic rate, and our results have varied. One patient showed an increased excretion of arsenic when sodium thiosulphate was administered, and improvement occurred when the arsenic disappeared. The thiosulphate is best given intravenously, but it may also be given by mouth in enterically coated tablets, which are about 60 or 70 per cent as effective as the intravenous medication.

DR. H. J. PARKHURST: This case bears some resemblance to one of dermatomyositis presented by Dr. Toomey before the Cleveland Dermatological Society in November, 1930, and reported in the ARCHIVES (**23**:589 [March] 1931). The condition of the skin of Dr. Toomey's patient markedly resembled that in scleroderma, and developed after scarlatina in a girl, aged 11. The skin was tender. The condition usually clears up in a few months, with or without the administration of thyroid. In our present patient the condition developed after a tonsillar infection, and it occurred to me that it may really have been dermatomyositis.

CLEVELAND DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Jan. 22, 1931

J. R. DRIVER, M.D., *Presiding*

LYMPHANGIOMA. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

S. S., a white man, aged 25, had previously been presented before the Society with an extensive lymphangioma of the left buttock, which had resisted seven attempted excisions and five filtered roentgen irradiations. On Dec. 30, 1930,

thirty-nine radium needles, representing a total of 78 mg. of radium, had been implanted in the upper half of the tumor and allowed to remain for one week. At the time of presentation, the treated area had lost its papillomatous appearance. Following the treatment the erythrocyte count had fallen from 4,000,000 to 3,000,000, and the hemoglobin percentage from 90 to 55.

DISCUSSION

DR. H. N. COLE: This patient has had a profound systemic reaction from radium: acidosis, anemia and fever. I think that these factors should be considered in choosing this type of treatment.

ACRODERMATITIS PERSTANS. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

I. G., a girl, aged 5, presented vesicular, pustular and crusted lesions on the fingers and palms of three months' duration and similar lesions, with a tendency to coalescence, on the soles of ten days' duration.

At the time of presentation, there were lesions at the tips of the fingers and on the right hypothenar eminence, consisting of ulcers, about 1 cm. in diameter, without a tendency to heal. On the toes and plantar surfaces, especially of the right foot, there were vesicles and pustules, and the skin was undermined, with an abundant serous exudate. *Staphylococcus albus* was found in cultures. The leukocyte count was 12,250, with 45 per cent polymorphonuclears, 51 per cent mononuclears, 2 per cent transitionals and 2 per cent eosinophils. Various antiseptic applications had been used constantly, without benefit.

DISCUSSION

DR. H. J. PARKHURST: The lesions on the fingers are those of acrodermatitis perstans, while those on the feet are characteristic of dermatitis repens. I think that these two conditions are closely related. There are a few small lesions on the legs, apparently secondary impetigo. I found no clinical evidence of parasitic disease.

DR. J. R. DRIVER: The eruption on the feet developed while the patient was in the hospital. The lesions on the fingers were considered as impetigo when first observed; later, they resembled granuloma pyogenicum, and pulsated. They were cauterized. The sister of the patient had typical impetigo of the face and hands at the time the patient was admitted. I consider it a case of dermatitis repens.

DR. H. G. MISKJIAN: The patient has an elevated temperature. Has a blood culture been made?

DR. H. F. DEWOLF: No.

DR. E. W. NETHERTON: Dr. Rauschkolb and I suggest that bacteriophage be tried. The lesions should first be thoroughly cleaned. I believe that this is a case of dermatitis repens, probably due to a staphylococcic infection.

GUMMA OF THE PENIS AND SCROTUM. Presented by DR. H. F. DEWOLF.

F. S., a white man, aged 45, from the service of Dr. H. N. Cole and Dr. J. R. Driver, had first noticed a painless "boil" near the base of the penis about three months previously. He had had a penile lesion twenty years previously, for which he had taken pills for a short time. An extensive, painless, ulcerative lesion encircled the penis and involved the anterior surface of the scrotum. Its borders were sharply outlined, and there was evidence of healing in the older parts of the process. The Wassermann reaction was strongly positive, while dark-field examination and smears for the bacillus of Ducrey gave negative results.

DISCUSSION

DR. R. E. BARNEY: This is an interesting condition. The tissue surrounding the ulceration is gummatous. In differential diagnosis, epithelioma and gumma would have to be considered. The absence of bleeding and pain is in favor of gumma, and the history of a previous penile lesion is also suggestive.

DR. H. N. COLE: Epitheliomas in this region are slow in development. A chancroidal infection is another possibility, but no Ducrey bacilli were found in smears.

DERMATITIS FACTITIA. Presented by DR. H. F. DEWOLF.

C. S., a Negro, aged 37, from the service of Dr. H. N. Cole and Dr. J. R. Driver, presented pruritic lesions on the scrotum, thighs, axillae and nucha of two months' duration. At the back of the neck there was a necrotic ulcer 5 cm. in diameter, with a trickle lesion at its lower border. Similar lesions were located on the anterior axillary folds and on the inner aspect of the thighs near the scrotum. The scrotum was covered with well defined ulcers bearing a thick yellowish exudate, and the ventral surface of the penis was distorted by old scars. Wassermann tests, smears for the Ducrey bacillus and Donovan bodies and dark-field examinations gave negative results.

DISCUSSION

DR. R. E. BARNEY: Clinically, the lesions are bizarre; they fit into no disease group. The lesion on the back of the neck shows evidence of trickling at the lower border, and the character of the patient points to a diagnosis of dermatitis factitia.

DR. W. R. JAFFREY (Hamilton, Ontario): These patients frequently present areas of anesthesia and a loss of corneal and epiglottic reflexes.

DR. H. N. COLE: I observed a similar case yesterday in a Negro with a lesion on the right arm of two years' duration, which followed a burn. He showed complete hemianesthesia.

DR. J. R. DRIVER: In this condition, symmetry of the lesions and mutilation of the genitalia have frequently been noted. This case demonstrates these two points very well.

DERMATITIS MEDICAMENTOSA (NEOARSPHENAMINE?). Presented by DR. H. F. DEWOLF.

In I. S., a Negress, aged 48, from the service of Dr. H. N. Cole and Dr. J. R. Driver, an eruption had developed in the right cubital fossa in December, 1930, after eleven injections, presumably of neoarsphenamine, had been given on account of a lesion on the right leg. Immediately after the twelfth injection, an extensive pruritic eruption had appeared. There was a widespread, symmetrical, sharply defined, dull red dermatitis. The face and neck were exempt. Most of the lesions were confluent, with scaling, weeping and fissuring. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. W. R. JAFFREY: On examining this patient, I considered the possibility of dermatitis herpetiformis or early pemphigus. The history, however, makes the diagnosis of arsenical dermatitis evident. There seems to be an allergic factor which produces lesions simulating those of seborrheic dermatitis. I have had good results from the use of sodium thiosulphate. It should be given early and in heavy dosage. I have had only one fatality from dermatitis caused by arsphenamine under this treatment.

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. H. F. DEWOLF.

E. T., a Negro, aged 33, from the service of Dr. H. N. Cole and Dr. J. R. Driver, presented a painful swelling in the right inguinal region of twenty-five days' duration, which had begun without any apparent cause. There had not been a penile sore, but the patient had had numerous exposures to venereal disease. The mass was bound down to the deeper tissues, and its summit was red and fluctuant. The base was very hard and showed a mild inflammatory reaction. No penile lesion was found. A cutaneous test for lymphogranulomatosis inguinalis was positive.

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. H. F. DEWOLF.

W. B., a Negro, aged 36, from the service of Dr. H. N. Cole and Dr. J. R. Driver, presented a penile sore and a swelling in the right groin. The sore had appeared eight weeks previously and the swelling one week later. There was an irregular, rather dirty ulcer, as large as a pea, on the dorsum of the prepuce. Its edges were raised and somewhat undermined, without induration. In the right inguinal region there was a large confluent mass, about 6 cm. in diameter, fixed to the underlying tissues. The Wassermann reaction of the blood was strongly positive, while dark-field observations and smears for the Ducrey bacillus were negative. A cutaneous test for lymphogranulomatosis inguinalis gave positive results.

DISCUSSION

DR. J. V. VAN CLEVE: These last two patients presented have almost identical histories. One gave no history of a penile lesion. The antigen used in the intradermal test was prepared by aspirating the bubo. The aspirated material was triturated with physiologic solution of sodium chloride. It was sterilized for two hours at 60 C. on the first day and for one hour on the second day. Cultures were then made for sterility. The tests were made on the forearms, as are intradermal tests in the tuberculin, and results were obtained within twenty-four hours. Thus far forty such tests have been made, and the results were positive in four cases in which the clinical diagnosis was lymphogranulomatosis inguinalis. One case of granuloma inguinale showed a positive result after forty-eight hours. Other conditions gave a negative response after twenty-four hours.

DR. H. N. COLE: That test was worked out in Jadassohn's clinic. It seems to be quite specific and is widely used in Europe. In 1925, Dr. Miskjian described the disease and called it hypertrophic bubo.

DR. H. G. MISKJIAN: In 1913, Nicolas and Favre described the inguinal adenitis that is now called lymphogranulomatosis inguinalis. Their description does not seem to cover the type that we see. They described nodules on the skin secondary to inguinal adenitis. There were multiple openings. In this country the usual manifestation is a mass that suppurates a little at the top. It does not exactly correspond with the condition described by Nicolas and Favre.

A CASE FOR DIAGNOSIS (PELLAGRA?). Presented by DR. H. F. DEWOLF.

C. C., a Chinaman, aged 45, from the service of Dr. H. N. Cole and Dr. J. R. Driver, had been addicted to the use of cocaine for many years, and stated that he had had an itching eruption every winter for five years. He was weak and emaciated. There was a generalized, exfoliative dermatitis, which was most pronounced on the face, trunk and upper extremities. The dorsal surfaces of the hands and wrists were deeply fissured, and an exuding dermatitis was present on the penis and scrotum.

DISCUSSION

DR. EMERSON GILLESPIE: Clinically, this is a case of dermatitis exfoliativa, with no history to account for it. The fact that the face and arms seem to be the parts worst involved, together with the patient's addiction to drugs, suggests that the dermatitis may be pellagroid.

DR. R. E. BARNEY: Clinically, the condition could be the pityriasis rubra of Hebra. There may be an underlying lymphoblastoma or tuberculosis.

DR. H. J. PARKHURST: The denuded condition of the tongue suggests pellagra.

DR. J. R. DRIVER: The patient also presents a weeping dermatitis of the axillae and perineum, which is frequently found in patients with pellagra. I consider it a case of pellagra.

DR. M. J. GIBANS: The hyperpigmented eruption is not sharply demarcated at the wrists.

TRICHOPHYTOSIS BARBAE (NODULAR TYPE). Presented by DR. E. W. NETHERTON.

A man, aged 24, a farmer, presented an eruption on the chin and cheeks, of five weeks' duration. There were six bright red, raised, soft, granulomatous nodules, the largest being at the angle of the jaw. They were smooth and dry, and the surface showed total alopecia. The regional lymph nodes were slightly enlarged. Numerous large spores were found about affected hairs, and a fungus was grown on culture mediums.

DISCUSSION

DR. C. B. NORRIS: I agree with the diagnosis. Recently I observed two cases in one family, and after visiting the farm on which the patients lived I traced the infection to cattle with a scaly eruption. In these cases I think it advisable to examine domestic animals in the search for the source of infection. Typhoid therapy seems beneficial.

DR. R. E. BARNEY: I was interested in this case because of the differential diagnosis between this condition and sycosis vulgaris. Trichophytosis barbae usually presents large granulomatous nodules, while in sycosis vulgaris the eruption is chronic, with numerous follicular papules that spread over the bearded region and do not produce the deep nodules that are seen in this case.

DR. W. R. JAFFREY: In Canada we often see these cases. Following the advice of Dr. Campbell, I have been using 1 drachm (3.9 Gm.) of phenol to 8 ounces (248.8 Gm.) of olive oil as compresses, with excellent results.

DR. E. W. NETHERTON: I presented this case because of the comparative rarity of the disease in Cleveland. In the past seven years no other case has been presented before this Society, and very few have come under my observation. I believe that Dr. M. F. Engman was the first to report excellent results following the use of typhoid shock in treating patients with this type of condition.

A CASE FOR DIAGNOSIS (GRANULOMA ANNULARE?). Presented by DR. E. W. NETHERTON.

A married woman, aged 27, in 1923 had had a condition suspected to be early tuberculosis, but no definite evidence of tuberculosis had been demonstrated. Her general health was good. She presented an eruption of seven years' duration, which had first appeared on the right elbow. New lesions had appeared from time to time on the dorsum of the right hand, the extensor surface of the right arm, the right shoulder and deltoid region, the lateral surface of each thigh and the anterior and inner surface of the right ankle. The lesions were of two types: (1) large, slightly violaceous plaques, which appeared to be made up of flat, shiny, annular papules, but which were really accentuations of the normal markings of the skin, without scaling and with hardly any palpable infiltration, and (2) dime-sized, fairly well outlined, circular, smooth, slightly infiltrated, yellowish-pink areas on the left ankle, the dorsum of the right hand and the extensor surface of the right arm and shoulder. One area on the shoulder consisted of a group of pinhead-sized infiltrations which were easily demonstrated under the diascope, and near this area was a yellowish-pink papule, the size of a match head, which seemed to be a primary lesion. The epidermis was normal. Scattered throughout the

corium were small, well defined areas of lymphocytic infiltration about the vessels and hair follicles. There were some small, sharply defined areas of epithelioid cells, a few fibroblasts and a moderate number of small lymphocytes, but no plasma cells or giant cells. Serologic tests and roentgenographic studies of the chest gave negative results.

DISCUSSION

DR. M. J. GIBANS: I consider this a case of lichen nitidus.

DR. J. E. FISHER: There are several annular lesions, especially that on the right shoulder, which would favor a diagnosis of granuloma annulare.

DR. H. N. COLE: I do not think that the lesions on the thighs can be diagnosed either as granuloma annulare or as lichen nitidus. For the rest of the eruption, I favor a diagnosis of granuloma annulare.

DR. E. I. STEINBERG: The lesions on the ankle are suggestive of scleroderma.

DR. J. E. RAUSCHKOLB: The histologic picture suggests granuloma annulare, and I suggest that gold sodium thiosulphate be tried. It has recently been used in a similar case with excellent results.

DR. E. W. NETHERTON: I consider this a case of granuloma annulare, on the basis of clinical and histologic observations. The clinical picture has been changed by roentgen therapy.

SARCOID (BOECK). Presented by DR. E. W. NETHERTON.

A man, aged 47, a painter, stated that three years previously he had first noticed a small brown nodule behind the right ear. It had enlarged, had recurred after excision and had again been excised. There were a few cutaneous nodules on the back and on the left arm of ten months' duration and one over the sternum and on the right ala nasi of a few weeks' duration. There had been no loss of weight and no subjective or constitutional symptoms.

In the fold behind the right ear there was a large, flat, somewhat nodular, dark brownish-red tumor, with sharply raised margins and a somewhat shiny surface presenting small telangiectases. The nodular portion occupied the postoperative scar. The regional lymph nodes were not enlarged. On the lateral surface of the left arm, midway between the shoulder and the elbow, there was a similar nodule as large as a coin of medium size. Scattered over the back and on the chest and nose there were pea-sized, yellowish-red, firm, cutaneous nodules, differing from the larger lesions only in size. Histologically, the epidermis was normal. In the corium there was a diffuse inflammatory infiltration with polymorphonuclear, eosinophil and plasma cells and large endothelial cells. Tubercles, giant cells and tubercle bacilli were not observed. The infiltration extended into the subcutaneous fat and involved the coil glands slightly.

The Wassermann and Kahn reactions were negative. Roentgen therapy had been employed without apparent benefit.

DISCUSSION

DR. J. E. RAUSCHKOLB: This case reminds me of the many instructive examples of Boeck's sarcoid which I saw at the International Congress in Copenhagen, Denmark, last summer.

DR. W. R. JAFFREY: Dr. Gray, of London, England, usually gives these patients sodium morrhuate, injecting 1 cc. of a 3 per cent solution twice weekly. He obtains good results.

TULAREMIA. Presented by DR. R. E. BARNEY.

H. H., a butcher, stated that on Dec. 28, 1930, he had suffered from chills, fever, prostration and vomiting. At that time he had noticed a painful ulcer just under the nail at the tip of the right middle finger, where he had been injured

by a fish bone. The finger had been immersed in a solution of mercuric chloride and small amounts of pus expressed; after four days involution occurred. At the onset there had been a painful swelling in the right axilla. The patient had been confined to his home for ten days with extreme weakness, a septic type of temperature and drenching night sweats; he had lost 6 pounds (2.7 Kg.) during that time. He stated that from November 15 until the development of the symptoms he had frequently cleaned rabbits. Tularemia had developed in one of his customers.

There was a pea-sized scar on the affected finger-tip and a plum-sized painless lymph node in each axilla. A specimen of the patient's blood had been sent to Dr. Francis in Washington, who found that it agglutinated *Bacillus tularense* in a dilution of 1 : 1,280, and *Brucella abortus* in a dilution of 1 : 20.

DISCUSSION

DR. E. W. NETHERTON: I agree with the diagnosis. In many of these cases an initial drop in temperature is followed by a septic temperature.

DR. R. E. BARNEY: I had wished to present another case of tularemia, but unfortunately the patient could not remain for the meeting. She was a Negress, aged 28, who had purchased a rabbit from this butcher. While cleaning the rabbit, she was aware of a scratch over the dorsal surface of the middle phalanx of her right index finger. Three days later a fever of 104 F. developed, with headache, vomiting, prostration and delirium. Two days after the onset of the constitutional symptoms, a small ulcer developed at the site of the scratch. There was also a painful axillary adenitis of the same side, which later fluctuated. A specimen of blood, which was sent to Washington, agglutinated *Bacillus tularense* in a dilution of 1 : 1,280.

NODULAR NONULCERATIVE GUMMAS. Presented by DR. R. E. BARNEY.

Mrs. A. T., aged 37, presented an eruption of two years' duration. Above the right knee and extending laterally into the popliteal space, there was a double palm-sized group of nodules, approximately the size of a pea, in arcuate configuration. They were dull red, deep-seated, firm and painless. There was a similar large coin-sized group of nodules just below the right knee. In the center of the larger group were numerous slightly elevated, yellowish plaques, varying in size from that of a glass pinhead to that of a pea, the surface of which, on close examination, showed an exaggeration of the cleavage lines of the skin and pinpoint depressions. Most of the plaques were angular in outline and were only slightly indurated. The Wassermann reaction was strongly positive. Glycosuria was absent.

Histologically, the nodules were found to be gummas, while the peculiar yellowish plaques showed dermal changes which required further investigation.

DISCUSSION

DR. H. N. COLE: I believe that the nodules at the border are gummas, in spite of their lack of great induration. I do not know whether the yellow lesions in the center are of the same character, but they suggest colloid degeneration of the skin.

Book Reviews

PRACTICAL RADIATION THERAPY. By IRA I. KAPLAN, B.S., M.D., Director, Division of Cancer, Department of Hospitals, New York, Attending Radiation Therapeutist, Bellevue Hospital. With a Special Chapter on Applied X-Ray Physics by Carl B. Braestrup, Radiation Physicist, Division of Cancer, Department of Hospitals, New York. Cloth. Price, $6. Pp. 354, with 227 illustrations. Philadelphia: W. B. Saunders Company, 1931.

In this book the treatments described are obviously the actual methods used by the author in his practice. He has a large experience, numbering about 2,000 cases annually, so that the book is a decidedly practical contribution. It has, however, a limited appeal to the dermatologist, for only about fifty pages are devoted to a consideration of conditions of the skin. The first third of the book is given to elementary principles: the history of the development of radiation, a description of the apparatus, the technic employed, a consideration of the applied x-ray physics and a chapter on dosages. The dermatologic conditions are then considered, and only the more common diseases are discussed. The list is not complete. Of the tineal infections, only ringworm of the scalp and beard is considered. Plantar warts are well treated; other types of warts are not considered, and conditions such as pyogenic granuloma, synovial lesions and mycosis fungoides are not mentioned. In places, the consideration of the common conditions lacks completeness. Concerning psoriasis, mention is made of roentgen exposures to the spine, but there is no reference to irradiation of the thymic areas; mention is not made of spinal roentgenotherapy for lichen planus. Of the acute infections, erysipelas is omitted.

The dermatologic descriptions are brief and, in general, inadequate. Of sycosis, the author says that "This lesion . . . presents multiple scaly sores." Filtered radiation is employed for almost all conditions of the skin. For epitheliomas, the author prefers radium, and the x-rays are merely mentioned. His results are apparently excellent, especially in cases of epithelioma of the lip; this section is particularly well illustrated. The paragraphs on keloids are excellent, but unfortunately illustrations are not shown. The book contains excellent photographs in black and white, with illustrations before and after treatment and accompanying notes stating the exact dosages of x-rays and of radium employed.

The last chapters are devoted to treatment with radiation in other fields, and the book is concluded by brief chapters on endothermy, nursing care of patients with malignant conditions, plans for a radiation therapy department for a general hospital and accidents and burns caused by radiation. In general, small dosages of x-rays are employed, and with radium, small amounts, heavily filtered over longer periods of time are advocated.

The book will undoubtedly prove useful, for it is a summary of the author's experience, but the section on dermatology is not as complete as it might be.

COLD IN RELATION TO SKIN DISEASES. By H. HAXTHAUSEN, Physician to the Finsen Light Institute, Copenhagen. Pp. 160. Copenhagen, Denmark: Levin & Munksgaard, 1930.

This monograph, which has been translated into English by Dr. W. Jenkins Oliver, gives a valuable statement of the influence of cold in the production of diseases of the skin. It is a broad and excellent treatment of the subject, and is, the reviewer believes, the first of its kind. The first pages are given to a brief review of the vascular supply of the skin. Then follows an account of the effects of cold on the skin and its vessels in normal subjects—the effects of different degrees of cold, of short contacts, of long contacts and of repeated contacts. The

author also takes up the effect of light as a complicating factor. There follows a consideration of perniosis, a term which the author uses as a collective noun that includes not only the ordinary erythema pernio, but conditions such as acrocyanosis, erythrocyanosis crurum and several other less familiar diseases of the skin that are dependent on the protracted action of cold. These conditions are all given brief historical consideration, and are then systematically considered in turn from the standpoint of etiology, clinical appearance, histopathologic pictures and treatment. The author groups them under the terms "perniosis" because they have similar vascular changes, but he distinguishes them by adjectives denoting the particular types: perniosis crurum, preniosis circumscripta, acroperniosis, etc. Eight pages are devoted to the treatment for these conditions, and the pertinent literature is critically reviewed. There is then an interesting chapter on the influence of perniosis in the development and distribution of other diseases of the skin. The author mentions specifically the exanthems of tuberculosis, erythema induratum, acneform tuberculids, lupus vulgaris, sarcoids and lupus erythematosus.

It is pointed out that these conditions occur particularly in perniotic areas or are exaggerated on the "cold areas." On the other hand, perniosis may exert a defensive action, so that the cold areas may appear relatively less susceptible than normal skin, as in certain syphilitic manifestations. The final pages are devoted to conditions such as livedo annularis and dermatitis hiemalis, and finally to the effect of cold on conditions such as eczema, Raynaud's disease and epidermolysis bullosa. The book contains a few illustrations in black and white. It has a full bibliography. It is the sort of book that is most welcome—a monograph on an important subject by one whose experience and researches in the field are so important as to make him a master of it. It deserves a place on the bookshelves of dermatologists.

HANDBUCH DER HAUT- UND GESCHLECHTSKRAKHEITEN. By PROF. RICHARD VOLK. Herausgegeben von J. Jadassohn. Volume 10. Part 1. Pp. 686, with many colored and black and white illustrations. Berlin: Julius Springer, 1931.

The reviewer received a preliminary copy of this volume on tuberculosis of the skin by Prof. Richard Volk of Vienna. He has already exhausted his vocabulary in praise of the various volumes in this encyclopedia as they have come to his attention. As would be expected of Professor Volk, his treatise comes up to the high standard of its predecessors. It has been developed on a comprehensive plan and is complete in detail. Every phase of tuberculosis of the skin is considered. One hundred pages are devoted to etiology; the tubercle bacillus, the toxins of tuberculosis, and the criteria to establish the tuberculous nature of a cutaneous disease are considered from every aspect. Another 115 pages are given to the pathogenesis of tuberculosis of the skin. Two hundred and twenty-five pages are given to the special consideration of the various manifestations of tuberculosis of the skin, and the therapeutic considerations are presented in 140 pages. Space, as usual in these volumes, has been allowed for the full development of every item in the consideration of the subject. The illustrations are not numerous, but they are excellent; particularly is there marked excellence in the colored pictures, both gross and microscopic. Only admiration can again be expressed for the spirit and scholarship contained in these volumes, and compliments are extended to Professor Volk for his masterly production.

Index to Current Literature

DERMATOLOGY

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Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: New Orleans. Time: 1932.

American Dermatological Association

C. Morton Smith, President, 437 Marlboro St., Boston.
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